THE BIOLOGY OF AGEING

Symposia of the Institute of Biology

BIOLOGICAL HAZARDS OF ATOMIC ENERGY
Oxford University Press, 1952

FREEZING AND DRYING
Institute of Biology 1952

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Symposia of the Institute of Biology, No. 6

EDITED BY

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and

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FOREWORD

THE Institute of Biology has from time to time organized symposia, and the papers read at five of these have now been published. The [illegible] broader than those which [illegible] ied journals, [illegible] peakers who [illegible] ooked on as [illegible] to make it difficult for [illegible] ies, and the five that have [illegible] n the shelves. It would [illegible] mposia were brought to- [illegible], what sometimes needs [illegible] cipline which can help in [illegible] understanding many aspects in the life of man. The Council of the Institute has accordingly decided that the symposia shall take the form of a journal, with the volumes to appear as far as possible annually. *The Biology of Ageing*, the volume for 1957, becomes [illegible] of the earlier volumes are set out on p. ii.

[illegible] have delayed publication unduly.

W. B. YAPP,
Editor for Symposia.

ACKNOWLEDGEMENTS

This volume is a record of the Symposium held at University [illegible] 1956. We thank [illegible] Professor W. J. E. Jessop); University College, London, for the use of the lecture theatre; and the Nuffield Foundation for a grant which enabled the papers to be printed and circulated before the meeting.

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CONTENTS

INTRODUCTION

By

F. LE GROS CLARK AND N. W. PIRIE

A SYMPOSIUM on ageing needs some introduction. The subject has about it a deceptive simplicity, but that is partly because we have tended to assume that ageing as we know it in man must in some way characterize any plant or animal that has lived long enough. Only of late years has the subject received much attention from research departments—and that for reasons that are all too human

Societies, such as our own, that contain a steadily increasing number of pensioners, were bound to grow more interested in the nature of [illegible]
delayed.
answers, t
probably inherent in the subject itself; senescence primarily means and always has meant *human* senescence, and human senescence is a [illegible]

A comment should be added on the terminology of the subject. The contributors to the symposium have been [illegible]
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used, and they appear tc
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th [illegible] may at any time prove lethal. Ageing must mean that organisms (though perhaps not all organisms) come to experience in the course of time a gradually *increasing*

liability to die, and often therefore to die from causes that might formerly have left them [illegible] ages in this sense does [illegible] viability until it has liv[illegible] may recognize or think we recognize such a senescent process at work in the members of many species of animals, we must not take for granted that the same deteriorative factors are at work in all of them. Indeed, to look for a cause of ageing common to all living things may be quite abortive. For one thing, it seems very probable that many organisms cannot be described as ageing at all Where ageing does occur in living things it should perhaps be treated, as Dr. Comfort has suggested, rather as a unity of effects than as a unity of causes. The factors that are operating may turn out to be too complex and too varied to allow of any neat biological classification.

The determination of the vulnerability of the members of an animal or plant population, with the passage of time, would be one way of measuring and comparing types of ageing All we should need to know would be the chronological ages of all the individuals at risk within our sample. They have, of course, to succumb before we know whether and at what rate their chances of dying have increased with their chronological ages. It has been more robustly suggested in the symposium that another method of tracing deteriorative changes could be adopted—that of measuring the working vigour of men and of some of their domesticated animals against the demands of fairly constant day-to-day tasks. If life tables can be constructed, why not "working-life tables"? The time of life at which working men or draught animals can no longer carry out [illegible] calculation based on mortality rates

A common-sense objection to measuring the degree of ageing in either of these ways is that they would often give a minimum not at birth but at some later age. For man, for birds and for many other animals the chances of dying are high in early life, and then fall to a minimum in what, in human terms, may be called late adolescence. There would be a similar, though less precise, maximum expectation of working life It is a matter for discussion and research to decide whether these facts would constitute a biological objection to a definition of ageing made in this way.

Since there is a distinctly human quality in the common ideas we have about senescence, several of the contributions to the symposium were confined to human aspects of the problem It would indeed be difficult to discuss the papers as a whole without making continual reference to the human implications of the subject. The contributions provide us with a brief survey of the biological problem of

ageing, as it is at present understood. Obviously what the writers

has, one might say, no more permanence than the vortex in an endlessly emptying bath that is being as endlessly replenished He interprets ageing in such an organism as a failure to make the absorption and retention of metabolites keep pace with losses due to leakage, the deficiency could occur either through a reduced absorption or through an increased leakiness. In the long run failures of this kind would make a cell unworkable, and he prefers

flowering ... by observers with such processes
which fl
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writers
philoso ... sexual manifestations promote ageing or inevitably precede its onset. This assumption runs through much of mediaeval and Calvinist thinking; and with Donne it even reached the dignity of poetry:

> "Since each such act they say
> Diminisheth the length of life a day."

Apparently this belief in the sex-influenced contraction of life, whether plant or human, was based less on any moral principle than on the idea that an organism must at last run through its allotted reserves of energy or lose the structural capacity for dealing with the energy it so gloriously expends. The idea that an organism lives till it has metabolized a definite amount of bodily energy is only a more generalized version of the same theme. Rubner, for instance, once surmised that the amount would ordinarily be about 200,000 kilocalories for every kilogram of an animal's adult body weight; he placed man in the exceptional position of being able to metabolize about four times as much as this. If that were so, man's place in nature would take some explaining. But Professor Bourlière shows below that things are not quite as simple as this, and that several *other animals are also exceptional. It may be true that the "rate* of living" of a species does in some way determine its average span [illegible] reduce their [illegible] non-hiberna- [illegible] eing used up [illegible] st know that [illegible] 's of lethargy that live longest; but it may be quite unjustifiable to compare them with bats.

Dr. Bourne reverts to the problem of the ageing of cells, this time as studied histologically within a multicellular organism. He describes changes in the mitochondria of cells, which in the main seem to result in an increased fragility; the cell, like the whole organism, finds, as it were, that its parts break more easily and repair less easily as it grows chronologically older. There are also more clearly definable changes going on within it, such as the accumulation of calcium, iron and pigments, and a variation in the concentrations of many of the enzymes. The effects of ageing in an animal's tissues are not readily studied because in many tissues the individual cells, [illegible] *onstantly renewed.* But in tissues [illegible] this kind there is a steady loss of cells, and this is perhaps most clearly seen in the central nervous system. Old age may, in fact, be due to an ultimately suicidal [illegible] organisms the process of ageing could thus be reduced to a single uniform causal sequence of events. Cellular changes of this kind [illegible]

people the most exasperating feature of old age is apt to be the decay of sexual capacity and enthusiasm, there is a tendency to overlook the fact that eunuchs often live to a ripe old age. The eunuch Narses

was well beyond seventy when he won his final battle against the Goths, and almost ninety before he was retired from the governorship of Italy. Dr Swyer surveys our knowledge of the changes in

preventing or counteracting some at least of the symptoms of advanced senescence. It is much to be hoped that this line of

though they tend to live longer than men, appear to suffer more from the disabilities that might well be remediable by this type of replacement therapy.

The notion that certain properties in a man's diet could conceivably prolong his life or vigour is no less ancient.

Dr. Comfort's paper on ageing in animals leads naturally to man. The impression we have of ageing in the animals with which we are most familiar is much the same as the impression of ageing as it is experienced by the members of our own species. Whether the complex of causes is invariably the same is another matter. We shall plainly not get much further until we possess detailed life tables for a number of species. It has been suggested in the course of the symposium that comparative information might be obtained by observations [illegible] and elepha[illegible] late in ind[illegible] use of the Burma forest elephant as a laboratory animal in the study of ageing offers some exciting prospects.

In his survey of the clinical aspects of senescence Professor Hobson brings into relief the fact that old age is frequently accompanied by chronic diseases and ailments of one kind or another. Dr. Heron emphasizes that in man at all events age is complicated by many psychological changes. Mr. Benjamin completes the human picture by displaying the vast and shifting demographic framework within which the drama of ageing is now being played out in our own country.

Our approach to the problems of senescence must necessarily be in some measure subjective, as indeed are the conceptions we tend to adopt about our own place in society when we arrive at a chronologically advanced age. How subjective our approach is, we can scarcely realize, so ingrained have become our traditional habits of thought. Most of us have our words and gestures perfect as we live through the Shakespearean Seven Ages of Man. Yet a biological residue remains which is clearly entitled to be called organic ageing. What precisely accumulates or breaks down or fails to function or runs out or goes to seed, we do not know, and it may be that none of these metaphors is strictly applicable. We do not know whether we shall later find ourselves describing these experiences in neurological or biochemical or cytological terms; the chances are that no one of the biological sciences will alone prove adequate to our purpose.

AGEING IN BACTERIA

By

C. N. HINSHELWOOD

Physical Chemistry Laboratory, University of Oxford

number of cells, and the masses of the various components, all increase according to an exponential law, and with the same rate constant for each.

$$n_t = n_0 e^{kt},\ (m_1)_t = (m_1)_0 e^{kt} \text{ and so on.}$$

The steady rhythm of growth and reproduction is seldom maintained for long, and indeed with cells such as bacteria, can only continue under rather carefully devised laboratory conditions. If one or

phase of exponential increase is upset. To understand the ways in which it is disturbed some attention must first be given to the kind of harmony which had been established during the preceding steady state.

of chemical syntheses there must be many sequences of consecutive reactions. These sequences must branch and interlock in a complicated scheme which constitutes the reaction pattern of the cell.

It is very unlikely indeed that there are individual substances capable of autosynthesis in isolation and in their own right. The process of self-duplication is much more probably the result of a co-ordinated interplay of reactions in which the products of one set of enzymes or cell constituents build up the material of another,

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processes which cause serious departures from the steady state set

disturbance has been.

rately co-ordinated activities.

The breakdown of glucose and other carbon compounds, so fundamental for the complete process of growth and multiplication, can of course be observed with suspensions of bacteria which are prevented from growing by the absence of any nitrogen source. The use of radioactive tracers shows that in the early stages of this

Bacterial cultures can be prepared by growth in media containing radioactive sulphur, phosphorus or carbon. The cells containing this labelled material can then be suspended in a medium lacking one of the essential components for growth, and as they sojourn here any exchange with the medium can be followed.

In these circumstances what is observed is slow ...

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The experiments can be inverted, with the active elements added to the external medium.

and so on in an interlocking system according to equations of the type

$$dX_1/dt=a_1X_2,\ dX_2/dt=a_2X_3 \text{ and so on.}$$

It is easy to show that in the steady state of such a system $dX_1/dt=kX_1$, $dX_2/dt=kX_2$ and so on, all the k's being equal, and the ratios X_1/X_2, X_1/X_3 . . . values. These ratios are maintai goes on in a constant medium. new medium where the relative rates of different individual reaction steps of the complex reaction pattern are changed, the cell automatically undergoes an adaptive modulation to a new set of ratios.

When the maintenance of the complete rhythm is interrupted by the failure of supplies, there is no necessity at all for all the individual reaction steps to cease simultaneously and they do not do so. After the fully co-ordinated working (which leads to increase in size followed by periodic division) has been upset many different things may happen to bacterial cells.

In some circumstances division may continue without increase in the tot

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Thus more is synthesized from somewhere. The necessary phosphorus has been shown in certain examples to be derived from the ribose nucleic acid already formed. Direct interconversion of ribose nucleic acid and deoxyribose nucleic acid being unlikely in the circumstances, a reversal of the condensation processes by which the ribose nucleic acid was originally formed seems to be involved. T used, for t ibly after s In other c shown to increase at the end of the lag phase to a steady level which is reached at the expense of inorganic phosphate in the medium and which is maintained during the logarithmic period. The level falls again as

been in balance continue in a less co-ordinated way. Even more significantly they indicate how certain synthetic processes (e.g. the deoxyribose nucleic acid formation) can occur by a re-allocation of the internal resources of the cell, made possible by a reversal of previous syntheses. This principle will prove of importance in what follows.

The consumption of labile intermediates, the re-distribution of material by degradation and fresh synthesis, the decay of enzyme systems, and sometimes actual lysis of parts of the cell. are all

substances. The exponential law is by no means exactly followed. Sometimes there is an initial period during which the death rate is quite low and it rises only after the adverse environment has had time to bring about progressive changes in the cells. Sometimes, on the other hand, there is a resistant tail of cells which survive much longer than the simple law would predict. But the exponential curve is often enough followed sufficiently closely for it to possess theoretical significance. At its face value such a law implies that the chance of death in a given short time interval for any cell is independent of its previous history, as in the well known phenomenon of the radioactive decay of atoms.

The interpretation given in the well known "target" theory is that some sensitive centre in the cell receives a random hit from a molecule of a toxic agent, or from a quantum of high energy radi-

that adequate experimental technique would reveal an early region of the decay curve where the chance of death increases with time, as is required by theories that the toxic agents cause progressive damage. Nevertheless, there is no doubt that the

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In one

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actual lys... localized parts of the material may set in, polymerization and condensation reactions may be reversed. But as some of these things happen, the internal medium of the cell is enriched by compounds containing carbon, nitrogen and other elements which can be used for the repair or

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the constit

Little actual uptake of the labelled elements is then observed. What occurs is thus *predominantly a slow one-way leakage but one which* involves essentially the living cells. The explanation seems to be as follows. There is a lively internal interchange of materials within the living but non-dividing cell, compounds formed by reversed synthesis in one part being more or less avidly salved for re-synthesis *in another (as in the example of the RNA→ DNA* conversion). The salvage mechanism is, however, not perfectly efficient and some of the intermediates leak slowly out. The time scale of the leakage is such that the experiments extend over a period which may vary from several days to several weeks.

Since radioactive markers began to be available for the investigation of the detailed balance sheet of reactions in cells and tissues,

permanence, are dissolved and renewed according to a time scale of days or weeks. It is true that this almost transatlantic zest for scrapping and replacement is not universal, nor so great that appreciable exchanges can be detected during the period of active growth itself. Spiegelman, Monod and others find that proteins do not turn over to any important extent during the actual growth of

less important in the existence of non-dividing cells.

is ad- ith of *Bacillus subtilis*. Bacterial spores achieve a relatively very stable non-dividing economy of low activity, but commonly the processes of

The process of ageing and death in a unicellular organism is one of great interest and the subject of much controversy. A large population of unicellular organisms declines with time according to a law $n=n_0e^{-\lambda t}$, where er at time t and λ according to the state of the environment and the presence or absence of toxic

of the previous history of the cell. The condition for the approximate applicability of the exponential decay law is then fulfilled.

This point of view, which stresses the dynamic nature of the

DISCUSSION

M. R. Droop. Does Professor Hinshelwood consider that there is any profit in the analogy between ageing in the metazoan organism and the bacterial culture as opposed to the bacterial cell?

In liquid cultures the bacteria are more nearly independent units but by no means completely so, and their mutual interactions are significant in several ways.

O. V. S. Heath. By appropriate modification of the

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In these conditions there could be an actual waxing and waning in the amounts of various enzymes or in the intensity of various functions of the cell. Something analogous is *mutatis mutandis* [illegible] or runs out. In the declining economy the chaos can be even worse. Some parts of the cell may even acquire phage-like properties and prey upon neighbouring parts.

In such circumstances the waxing and waning of given pairs of enzymes, or types of cell material, might be likened to the changes of various animal species some of which prey upon others. In competitive systems of this kind, as Volterra showed, periodic changes in the numbers of the various species may be set up. When one species has plenty to prey on, it multiplies, and then consumes the prey so fast that this becomes scarce. Then there is a shortage of food for the predatory species which in turn declines while the prey has a fresh opportunity to increase. [illegible]

truly periodic with the cycles repeating themselves exactly, since this state of affairs would demand the fulfilment of rather precisely defined conditions, but a rough periodicity is quite plausible.

The periodicities will be multiple, applying to various pairs of cell units which can enter into relations analogous to those of predator and prey.

These various periodicities, moreover, will be largely independent of one another with their phases randomly related. In the declining cell economy there is no mechanism of adjustment, as there is in the gradual establishment of logarithmic growth, for harmonizing the amounts of the constituents with the various relevant rate con- [illegible] state.

[illegible] associated enzyme activities [illegible] and with independent frequencies, there will exist a certain probability that different functions (amounts or activities) will pass within a given short interval of *time through a minimum value together. This probability* is independent of the previous history of the cell, just as the chance in a radioactive atom of that conjunction of events leading to disintegration is independent of time.

Suppose now that when a given number of cell functions simultaneously drop to a minimum, viability is irretrievably impaired, that restitution becomes impossible and that death ensues. *Then the chance of death in a given interval of time is more or less independent*

AGEING IN HIGHER PLANTS

By

O. V. S. HEATH

Research Institute of Plant Physiology, Imperial College London, S.W.7

THE mode of growth of higher plants differs so fundamentally from that of animals that the problems of ageing may be expected to differ in like degree. A perennial plant, such as a dicotyledonous or coniferous tree, has all the working parts continually renewed, in

meristem (or embryonic zone) and from subsequent extension of the new cells so formed; the growth in girth arises mainly from new cells formed by a continuous meristematic layer, the cambium, which develops a short distance behind the terminal meristem and completely surrounds the shoot or root as the case may be. This

growth in length but produces a succession of primordia which

not seem to play any active part in the life of the tree.) Thus the

Sequential changes in the kinds of leaf produced by the meristems

It is well known that the early leaves of many plants show "youth forms", often of simpler shape or with better developed laminae than those formed later. This may apply to plants grown from cuttings as well as to those grown from seed. Thus cuttings of the hare-bell (*Campanula rotundifolia*) revert to the rounded leaf [illegible] for the first few new leaves, the later ones being linear. Early [illegible]

[illegible] flowers (see below). In many cases a [illegible] form" can, however, be produced by manipulation of external factors. Thus the hare-bell can be made to produce rounded leaves by low light intensity and the shrubby veronicas of New Zealand will produce leaf blades, which they lack in the mature form, in response to high humidity. The retention of the broad "youth form" of leaf by eucalypts grown in this country may be due to the same factors of low light intensity and high humidity. The fact remains that external factors cannot, apparently, *prevent* the [illegible] of "youth forms" in early formed leaves and thus a [illegible]

[illegible] al meristem" in some [illegible]

[illegible] modified by manurial deficiencies (Gregory and Richards, 1929); in the fully manured plants each rate for the last-formed (10th) leaf [illegible]

growth in some respects resembles reproduction, for the tree will have become an entirely new individual in the sense that a plant from a cutting or a tissue culture transplant is a new individual. The tree is in fact not unlike a coral colony though a much more *highly organized "symbiotic community" (J. E. Baker) and apart from* accident, disease and some mechanical and nutritional considerations there seems no reason why it should not live indefinitely. The giant redwood trees of California (*Sequoia gigantea*) show that this is not far from the truth, for specimens are estimated to have lived for some 3,000 years, attaining a height of over 300 feet and a diameter at breast height of 24 feet. Specimens of swamp cypress (*Taxodium mexicanum*) are estimated to be 4,000 years old.

It would seem that the meristems should be ageless as they are renewed continually. Nevertheless they are found to show systematic changes with time and although some of these are undoubtedly caused by external factors others seem to be due to internal factors [illegible] of the *cambium*, which [illegible] ood", thus forming the [illegible] e intimately connected [illegible] 1951). Some tropical timbers grown in non-seasonal climates show no annual rings, but even so there is normally a pause in cambial activity with the shedding of leaves and a renewal of activity with the expansion of new leaves (Simon, 1914, Coster, 1927–8 both cited by Richards, P. W., 1952 [illegible] terminal m [illegible] controlled [illegible] appear to [illegible] selves seem to be subject to inherent changes with time, not only in the periodical production in perennials of new leaves and of flowers but also, especially perhaps in annuals and biennials, in the kinds of leaves produced. In the latter types of plant the change over from purely vegetative growth to reproduction is associated with profound changes in the terminal meristems and is followed, after fruiting, by death; even in perennials there is normally, with the first onset of flowering, a marked check to vegetative growth and to the activity of those terminal meristems which remain vegetative.

The main problems of ageing in higher plants are thus, *in order of increasing importance:*

(*a*) The ageing and shedding of individual organs.
This is intimately bound up with

(*b*) Inherent changes in rate of leaf production.

(*c*) Inherent changes in kinds of leaf produced.

(*d*) The change from purely vegetative growth to reproduction.

Discussion of the first two of these problems is omitted owing to lack of space.

terms of total dry weight the "efficiency index" since it measures the efficiency with which the plant uses its "capital" as repre-

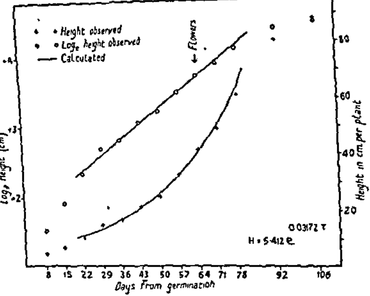

FIG. 1.—Approximately exponential growth in *height* of main axis of cotton at Barberton, South Africa, season 1933–4. (From *Annals of Botany*, N.S., 1, 1937, p. 517.)

growth of the hypocotyl making use of reserves from the cotyledons. It may be noted that the relative growth rate in terms of height (a linear measure) is one-third of that in te

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simple age series. The variation from leaf to leaf may often be much greater than the change with age in any one leaf. The apparent " age drift " obtained from such a series of successive leaves is compounded of the effects of the positions of the leaves on the plant and of their ages; it bears no simple relation to the true time drifts for individual leaves nor to the mean time drift for all the leaves. This warning is still frequently ignored.

The change from purely vegetative growth to reproduction

Some aspects of this change will be considered in rather more detail and since it greatly affects growth rates a preliminary consideration of growth relations may be useful.

In higher plants the rate of growth in dry weight at an instant will be the net gain represented by the difference of the rate of assimilation (X) and the rate of respiration (Y); it will be completely determined by:

1. The assimilation rate (per unit leaf area) $= x = \frac{X}{A}$
2. The respiration rate (per g. of total dry weight) $= y = \frac{Y}{B}$
3. The ratio of leaf surface to total dry weight $= \frac{A}{B}$
4. The total dry weight itself (B) which together with *3* specifies the leaf area A.

If the first three were to remain constant over a period, then the assimilation rate would also be constant if expressed per unit of total dry weight (in view of the constancy of *3*); hence the net gain per unit of total dry weight would be constant, i.e., the rate of increase in dry weight would be proportional to *4*, the dry weight already achieved. The *relative growth rate* would thus be constant and growth would follow an exponential curve (Blackman, 1919). Since plant growth is largely a process of cell multiplication, this is the curve to which it will tend *if* all the cells, or a constant proportion of them, continue to divide and *if* they do so at a constant rate, i.e., if growth continues unrestricted by internal or external factors. It seems most improbable that either of these two provisos would be fulfilled for any long period. Further, in view of the differences in assimilation rates and respiration rates of successive leaves already noted, and of the mechanical necessity for a greater proportion of supporting tissue as the total leaf surface enlarges, it seems equally improbable that the values of *1*, *2* and *3* above would remain constant. Nevertheless it is found in many cases that the relative growth rate *is* nearly constant, falling very slightly until flowering ensues when a sharp drop occurs. This was noted by Blackman in the paper cited and he called the relative growth rate in

crease in efficiency index.

TABLE 2.—(from Heath 1937*b*)

Mean quadratic regression coefficients (14-day) for logarithms of total dry weight and of leaf dry weight

Season	*Total weight*	*Leaf weight*	*P**
1933–4	—0 0587	—0 0751	0 001
1934–5	—0 0464	—0 0545	0·1—0·2

*P=probability of the difference between the two measures being due to chance.

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(C ... case especially will be considered here. Crowther postulates a " self-regulating mechanism " essentially as follows:

In the early stages of growth there are few positions where buds can form

produced. Boll (fruit) development followed with the resultant ... larger the number of flower buds it severe drain on nitrogen and also carbohydrates. Growth then ceased, and many of the flower buds and bolls were shed. Crowther

exhibit a small but significant downward trend, as shown by the quadratic regression of log {total dry weight} on time (Table 2). Since net assimilation rate showed no downward trend, this fall in

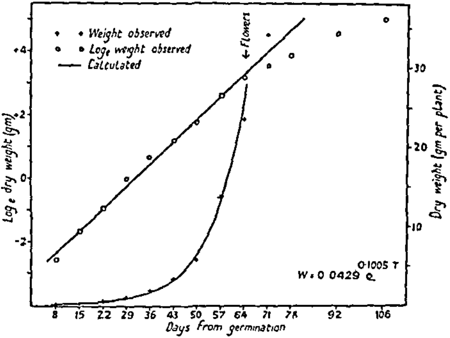

FIG. 2.—Approximately exponential growth in total dry weight of cotton at Barberton, South Africa, season 1933–4. (From *Annals of Botany*, N.S. 1, 1937, p. 517.)

efficiency index had to be attributed to a marked decrease which occurred in the ratio of leaf to whole plant (Table 1; data for two seasons are included).

TABLE 1.—(from Heath 1937*b*)

Leaves as percentage of total dry weight of shoot

Season	*Initial sample*	*At flowering*
1933–4	77·0	54·7
1934–5	74·9	56·4

ound that simultaneously with the rapid transference of nitrogen

of the cotton plant show clearly that much or most of the nitrogen for the bolls is withdrawn from the leaves. Nevertheless, the check to growth which occurs with the onset of flowering does not appear to be solely a nutritional effect. In Fig. 3 are presented hitherto unpublished data for the mean (absolute) growth rates in height of 45 normal cotton plants and also for 45 similar plants on the same plot from which all flower buds and developing monopodial lateral

days) of this period had no noticeable effect on the growth rate of the

normal plants ceased growth (24.3.31) it followed a trend almost identical with that of mean air temperature The curves shown for growth of the disbudded plants and mean air temperatures are fourth degree polynomials The total correlation between the

and correspond

a value of *r* of

seems clear th

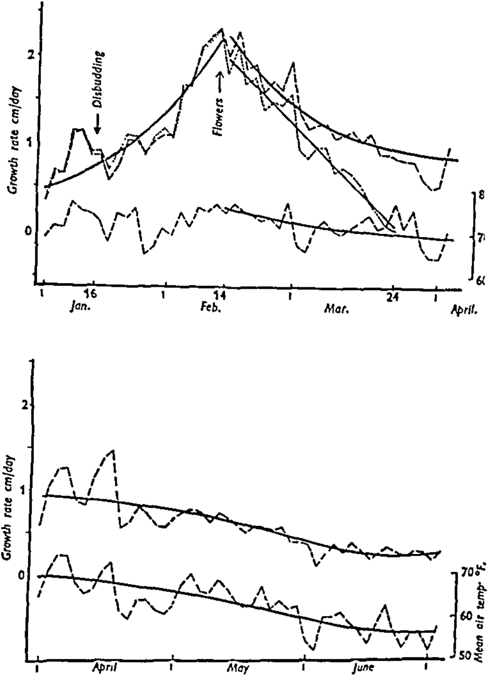

FIG 3.—Absolute growth rates in height of main axis of "normal" and "disbudded" cotton plants; also mean air temperatures, Barberton, South Africa, season 1930–31.

plot from which all flower buds and developing monopodial lateral shoots were removed every alternate day, when all the plants were measured In the disbudded plants, then, the nutritional strain

days) of this period had no noticeable effect on the growth rate of the disbudded plants Following first flower opening the growth rate of the normal plants fell almost linearly to zero in 40 days; *the growth rate of the disbudded plants fell from the same date*, scarcely less rapidly for the first three weeks, and from the time when the

at the time for first flower opening, even in the absence

inherent change in the

nature. Data for disbud

more than four weeks before first flower opening in the experiment just considered. However, since barley is a monocotyledon with a terminal inflorescence and cotton a dicotyledon with a system of sympodial lateral flowering shoots some other differences in organization may also be expected.

Finally, the "minimum leaf number", found before the occurence of inflorescence initiation in certain plants with terminal inflorescences, may be briefly discussed. Klebs (1918) postulated that until a plant had reached a certain stage of development and was "ripe to flower" no combination of environmental conditions could make it flower; after this stage it would flower in response to appropriate external-conditions only. Clearly, if such a stage is rigidly defined it may at any time be disproved by the experimental exploration of new combinations of conditions, like any other null hypothesis. Thus Purvis (1934) and Purvis and Gregory (1937) found that in rye the number of leaves preceding the terminal inflorescence could be increased by environmental conditions up to about 25, but could not be reduced below seven. This was therefore accepted as morphologically defining the stage of "ripeness to flower". Much later Gott, Gregory and Purvis (1955) found that this number could be reduced to five by the use of continuous illumination. As the rye embryo already has four leaf primordia in the ripe grain and another develops during sprouting, this raised the possibility that the plant was "ripe to flower" immediately after germination and as soon as the first leaf emerging was exposed to light By prematurely harvesting grain, dwarf embryos were obtained with as few as two or three leaf primordia but the minimal number of leaves formed before flowering was still five. This was taken as evidence for an obligate vegetative stage, represented by the development of five leaves, which must precede flowering.

In the onion the minimum number of leaves and scales so far found before flowering is about 13 (Heath and Holdsworth, 1948) and this leaf number may perhaps represent an obligate minimum for "ripeness to flower". There is, however, a marked effect of [illegible] plants prevented [illegible] 1950) or plants [illegible] The evidence suggests that initiation follows when the plant has attained a sufficient size, and the temperature is sufficiently low (a mean of about 12°C.), irrespective of *total* number of leaves and scales produced or of whether the plant has formed a bulb It is most unusual for inflorescence initiation to occur in onion sets (small bulbs) formed from plants which had fewer than five *emerged* leaves and this may well be a matter of integrated leaf area. Experimental evidence was obtained for the production of an inflorescence-promoting hormone, produced in the emerged leaves, stored in the swollen leaf bases formed when bulbing occurred and transferred slowly to

the growing point during winter storage. Small sets when ripe normally have no swollen leaf bases but only swollen scales; larger sets and bulbs such as normally initiate inflorescences have one or

elsewhere in the bulb

Thus in the onion the effect of age on inflorescence initiation would seem to operate mainly through size attained (possibly leaf area) and if there is an obligate minimal leaf number it is generally exceeded

There is no lack of interesting examples of apparent age effects on the change from vegetative growth to reproduction, *for instance* the simultaneous flowering after many years of a plantation of Sisal (*Agave sislana*) followed by death of the plants, but it seems more fruitful to discuss experimental work when one is aware of its existence.

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DISCUSSION

Elizabeth Wangermann. There is more convincing evidence about [illegible]

any loss in growth potential, under constant and favourable conditions. (Some of my plants have now been growing for five months at the same rate, and look like continuing indefinitely.)

It seems therefore that ageing changes at the meristem occur in some groups of plants but not in others, and each will have to be investigated separately.

event such as pollination.

The question of the mechanism of translocation of carbohydrate seems to me to be concerned. It may be that the

O. V. S. Heath. Although the flower buds may have had a high percentage nitrogen content the total weight of buds was very small as they

I agree that the contrast between the continued growth over many months of the disbudded plants and the rapid fall of the
zero in the case c
in nutrition brou
think, however,
of growth, which
plants, can be a
sudden systemat
Possibly hormon

P. C. DeKock. Results obtained at the Macaulay Institute show that, in ageing leaves, the phosphorus/iron, potassium/calcium and citric acid/malic acid ratios decrease, as do also the respiration rate and the sensitivity of respiration to inhibitors, ageing leaves often showing a stimulation of respiration in their presence This has been found for *successive leaves on a shoot, as well as for the same leaf sampled at various* times (tobacco, larch). There is considerable evidence to show that essentially similar changes in mineral composition, organic acids, respiratory rate and sensitivity to inhibitors, take place in all animal cells.

H. W B. Barlow May I present some of Mr. A. C. Mason's results relating to the effects of age and leaf position on the mineral composition

[illegible]

curves obtained during the period of shoot elongation and those obtained when growth had ceased The latter set of samples shows the effect of

[illegible]

achieved being least in the lowest temperature, (*b*) the curves for extension in pure water and indoleacetic acid at 10, 20 and 30° C. show that temperature and growth substance are to some extent interchangeable, the 20° C. water curve being very similar to that for 10° C in indoleacetic acid.

When growth is rapid, extension is a good index of "age", but at lower temperatures extension is slowed down more than "ageing", so that these sections never attain the final length of those at higher temperatures.

Sections transferred from low to high temperatures never catch up [illegible] water [illegible] water; [illegible] ch up [illegible] well as extension has been arrested.

AGEING IN ANIMALS

By

ALEX COMFORT

Nuffield Research Fellow, Department of Zoology, University College London, W.C 1

AGEING is the name given to the progressive decrease in vigour [illegible] in some organisms with the passage of time, leading [illegible]

death increases with age, so that these forms have characteristic maximum life-spans In animals not subject to ageing, the probability of death would not increase, and the life span, though finite, would be indeterminate.

[illegible]

continuously and have no fixed maximum size Animals of sharply-fixed cell number which have no regenerative powers (rotifers, nematodes) tend to have an equally sharply-limited life span. One determinant of ageing may thus be the possession of cells which cannot be renewed by division and which deteriorate in the course of metabolic life Mammalian age processes may well, however, involve the production of new cells differing in quality and in responses from those which they replace Wear in irreplaceable structures such as teeth and wings, processes of accumulation, processes of depletion [illegible] effects of r[illegible] animals [illegible] effects rather than a unity of causes.

The rate of progress of age changes is a function not primarily of the passing of time but of developmental or metabolic activity (the "rate of living") [illegible] prolon[illegible] the an[illegible] has sh[illegible] the immaturity of rats is prolonged by underfeeding, the animals can be kept fully active, but juvenile, for their normal lifespan and then re-started in growth, the time gained in

marking time effectively doubling the length of life. The life of rats once sexually mature cannot be prolonged to anything like the same extent (McCay *et. al.*, 1941). These findings suggest that actuarial [illegible] metabolism just as growth [illegible] dpole. If this is so, one of [illegible] search is to determine the components of the "programme" of mammalian development [illegible]

[illegible]

different types of vertebrate, so that age processes could be correlated with other physiological events. Such figures have been [illegible] nts, and one [illegible] There has [illegible] xistence for captive birds, whose longevity is known to be much greater in proportion than that of mammals similar in size and activity. In some cases there are large differences in rate of development and life-span between animals of closely related species which could profitably be investigated if better actuarial data were forthcoming.

One consequence of this lack of information is that we have no experimental mammal, intermediate in size and longevity between man and the small rodents, whose rate of ageing is accurately known. There are no published actuarial tables for rabbits or dogs, and only incomplete information for guinea pigs (Rogers, 1949). In consequence, many descriptions of physiological differences between "young" and "old" animals are in fact descriptions of differences between infants and youngish adults.

Apart from a limited number of species whose ages can be deter- [illegible] ich as scales [illegible] vertebrates [illegible] ude kennel-books and stud-books, notes kept by breeders, and the files of zoological gardens. Such material varies greatly in quality, and in most cases there are substantial losses to the record from sale, culling, or deliberate killing in the course of experiment In spite of this, it has already been possible to obtain from these sources partial life tables for several breeds of dogs, and for a number of mammals and birds in zoological gardens. It is a common character of many of these mammalian populations that the curve of decline is almost arith-linear, and the distribution of age at death is therefore rectangular, a constant number of individuals dying in unit time (Comfort, 1956b and 1957). In dogs, figures for Pekingese, mastiffs and wolfhounds indicate a more rapid senescence in the [illegible] an and maximum ages of these [illegible] per cent from those recorded [illegible]

Wild populations of small birds and mammals, and of many insects, commonly behave as if they were ageless, because the [illegible] as to be effectively age-independent, [illegible] Haldane (1953) [illegible] studies that the [illegible] increasing age. [illegible] vertebrate and [illegible] specific age in [illegible]

[illegible] factor of all the ageing processes is that [illegible]

contribution to the next generation of progeny has been made. Where few animals survive into late life, postponement of the expression of adverse genes may be equal in selective value to their complete abolition, and factors such as cessation of growth may be selected if they improve survival at the most fertile period of life, in spite of adverse effects in later periods Weismann originally [illegible]

might have been expected to be of selective advantage.

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marking time effectively doubling the length of life. The life of rats once sexually mature cannot be prolonged to anything like the same extent (McCay *et. al.*, 1941). These findings suggest that actuarial senescence is dissociable from total body metabolism just as growth and metabolism are dissociable in the tadpole. If this is so, one of the most important problems of age research is to determine the components of the "programme" of mammalian development which act as timekeepers in initiating the senile decline.

It might become easier [illegible] for the greatest possible [illegible] different types of vertebr[illegible] lated with other physiological events. Such figures have been available among vertebrates [illegible] nts, and one or [illegible] There has bee[illegible] existence for captive birds, whose longevity is known to be much greater in pro- [illegible] be investigated if better actuarial data were forthcoming.

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Apart from a limited number of species whose ages can be determined by inspection of annually-increasing structures such as scales or horns, it is evident that studies of ageing in long-lived vertebrates must be based chiefly on existing records. These include kennel-books and stud-books, notes kept by breeders, and the files of zoological gardens. Such material varies greatly in quality, and in most cases there are substantial losses to the record from sale, culling, or deliberate killing in the course of experiment. In spite of this, it has already been possible to obtain from these sources partial life tables for several breeds of dogs, and for a number of mammals and birds in zoological gardens. It is a common character of many of these mammalian populations that the curve of decline is almost anti-linear, and the distribution of age at death is therefore rectangular, a constant number of individuals dying in unit time (Comfort, 1956b and 1957) In dogs, figures for Pekingese, mastiffs and wolfhounds indicate a more rapid senescence in the large than in small breeds; the median and maximum ages of these pedigree breeds differ by less than 20 per cent from those recorded in dingoes and in wolves.

AGEING AND METABOLISM

By

FRANÇOIS BOURLIÈRE

Laboratoire de Physiologie, Faculté de Médecine, Paris

A LIVING organism being, as von Bertalanffy (1949) so aptly defined it, a graded structure of open systems which maintains itself in accordance with its inherent principles while its constituent elements are constantly changing, one may ask if the rate of renewal of these

in poikilothermic invertebrates and vertebrates, which lack the efficient thermoregulating and other homoiostatic mechanisms which keep the milieu intérieur of homoiothermic vertebrates so remarkably constant and almost insensible to the usual variations of their environment. In such lower animals, the conditions which are theoretically able to modify the energy-turnover are numerous. The first to be considered—and the first which has been studied experimentally—is the environmental temperature. But many other

Such a susceptibility to the variations of the environmental conditions is nevertheless not restricted to the "lower" animals.

some Insectivora and lower Primates) and the ageing processes of such abnormal forms are well worth investigating from the stand-

Invertebrates

In spite of the scarcity of information on ageing processes in invertebrates a few well established facts seem to indicate that there is among them a definite and inverse relation between metabolic rates and speed of growth, and duration of life.

DISCUSSION

W. B. Yapp. Could Dr. Comfort tell us a little more of his reasons for making two statements which go rather beyond the evidence that he has presented to us? The first is that we have no life tables for birds, whereas there are in fact several for wild populations, so that he seems to imply the assumption that a life-table is only of value when it applies to captive animals. The second is that while it is probable that birds potentially suffer from old age some cold-blooded vertebrates may not; the life-tables of wild birds provide no evidence for the first part of this view, while the anecdotal evidence of long-lived reptiles and fish mean nothing more than that the potential maximum age is high.

A. Comfort. There are in fact life tables for birds in the wild, but it is *not possible to study senescence in populations which do not live long* enough to reach senescence. There is no life table for birds under protected conditions; and so far population work on birds such as the albatross, which probably reach senescence in the wild, has not been in progress long enough to be of significant use to us. I think it will probably prove to be correct that the majority of poikilotherms ultimately undergo senescent change. *If we were to find animals in* which the potential life-span were so long that it could never be exhausted by any significant number of animals in a population, enquiry about their potential senescence would be a little academic. Perhaps I may take indeterminacy of age to mean simply the behaviour of animals in which no increase in vulnerability with age has been detected however long they have lived.

J. L. Cloudsley-Thompson. Insects and other terrestrial arthropods kept at constant temperatures tend not to live so long as control animals in fluctuating environmental conditions The subject has recently been reviewed (Cloudsley-Thompson, J. L., 1954, *Entomologist*, 86, 183–9). [illegible] hour periods [illegible] so rapidly (Cloudsley-Thompson, J. L., 1953, *Ann. Mag. Nat. Hist.* (12), 6, 705–12.

R. L. Worrall. Since old people, generally speaking, have less protein than when they were young, there must be an overall excess of protein combustion over protein intake, for the period of adult life as a whole This long-term net loss of body protein is too gradual and intermittent to be [illegible] balance investigations. If a man con- [illegible] mental error in nitrogen balance studies.

It is possible, however, to estimate the tendency of human adults towards protein deficiency, by measuring the percentage of total basal [illegible] protein combustion. I have published [illegible] ings of [illegible] protein in human adults can be minimized, so that a serious degree of tissue atrophy is postponed, and *active life is thus prolonged.*

AGEING AND METABOLISM

By

FRANÇOIS BOURLIÈRE

Laboratoire de Physiologie, Faculté de Médecine, Paris

A LIVING [illegible] it, a [illegible] accor [illegible] are cc [illegible] eleme [illegible] k[illegible] the milieu intérieur [illegible] other homoiostatic [illegible] lack the ably constant and almost insensible to the usual variations of their environment In such lower animals the [illegible] theoretically able to [illegible] first to [illegible] mentally [illegible] factors a [illegible] and food consumption, hibernation, aestivation and reproductive activities are all able to influence the rates of vital processes. [illegible] account. Seasonal changes of activity [illegible] many other

Such a susceptibility to the variations of the environmental conditions is nevertheless not restricted to the "lower" animals Temperature variations for instance may have an obvious influence on the metabolism of some birds (swifts, nightjars and humming-birds) and mammals (most marsupials, edentates, bats and even some Insectivora and lower Primates) and the ageing processes of such abnormal forms are well worth investigating from the standpoint of comparative gerontology

It is the purpose of this paper to review briefly the evidence at hand on the correlation which seems to exist in the animal kingdom between the rates of energy-turnover and ageing.

Invertebrates

In spite of the scarcity of information on ageing processes in invertebrates a few well established facts seem to indicate that there is among them a definite and inverse relation between metabolic rates and speed of growth, and duration of life.

DISCUSSION

W. B. Yapp. Could Dr. Comfort tell us a little more of his reasons for making two statements which go rather beyond the evidence that he has presented to us? The first is that we have no life tables for birds, whereas there are in fact several for wild populations, so that he seems to imply the assumption that a life-table is only of value when it applies to captive animals. The second is that while it is probable that birds potentially suffer from old age some cold-blooded vertebrates may not; the life-

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towards protein deficiency, by measuring the percentage of total basal

in human adults can be minimized, so that a serious degree of tissue atrophy is postponed, and active life is thus prolonged.

dividuals

animals was on the other hand distinctly abbreviated and the duration of life of the imago (which never takes food) remained unchanged. It thus appears that the prolongation of l
by intermittent starvation c
Subsequent experiments by
over show that food restric adult *Drosophila melanogaster* never increases the imaginal l

that they are kept in a suitable (moist and not too hot) environment.

Among rotifers the life span of the adults seems likewise to be inversely proportional to metabolic rate. Encysted adults may survive as long as 59 years in diapause (Rahm 1923)

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MacArthur and Baillie (1929*a*) used parthenogenetically produced males and females of one pure line of *Daphnia magna* and kept them at various temperatures (8, 10, 18 and 28°C.) the other conditions remaining constant. In such experiments the mean length of life of these cladocerans was strongly influenced by temperature. The correspondence between mean life-span and temperature is illustrated by the following figures: 25·586±0·28 days at 28°C., 41·675±0·35 days at 18°C., 87·8±1·98 days at 10°C. and 108·18±2·43 days at 8°C. The temperature coefficient for longevity averaged 2·12, which closely approximates that for most chemical reactions, but the Q_{10} values were higher (2·59) in the lower ranges and lower (1·64) in the higher ranges of temperature. It is to be noted also that the duration of life in males responded more sensitively and more extremely to temperature alterations than did that of females.

At the same time MacArthur and Baillie (1929*b*) found that elevation of temperature from 8 to 18°C. increased the heart rate and the susceptibility to potassium cyanide by a little over two and a half times, and this acceleration of metabolic rates was associated with a very nearly proportionate decrease in duration of life. It was also noted that the duration of life of females exceeded that of males, corresponding to a sexual difference in metabolic rates.

These results are confirmed by the findings of Terao and Tanaka (1930) on another cladoceran *Moina macrocopa*. The maximum duration of life of this species takes place at about 15°C. (14·36±0·38 days), and gradually decreases at higher temperatures (9·28±0·18 days at 21°C.; 6·51±1·67 days at 27°C.; 4·77±0·06 days at 33°C.). It is interesting to note that below 15°C. the life-span does not increase any more.

Alpatov and Pearl (1929) have investigated the effect of the temperature during development and imaginal life upon the duration of life of *Drosophila melanogaster*. Their results show that the effect [illegible] tures and in both sexes, with but one exception. For instance females reared at 28°C. had a mean duration of life of 28·52±0·34 days, while the ones reared at 18°C. lived 70·61±0·98 days. The [illegible] upon the duration of life [illegible] he environmental tempera- [illegible] a shorter time. This last [illegible] xperiments by Loeb and Northrop (1917).

Another experimental way to influence the metabolic rate of invertebrates is by food restriction. Such a method has been widely

and reptiles being less
data
) has
on on
nevertheless given us recently some very interesting
north American species.

The duration of the larval period of some widely distributed toads varies greatly with latitude In North America the bullfrog (*Rana catesbeiana*) undergoes metamorphosis at the end of the first
the extreme northern part of its range

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altogether different

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tural
the lizards

they grow throughout their short life-span On the other hand,

be determinate in one part of the animal's range and indeterminate in another.

Similar data are lacking for snakes and turtles, most unfortunately since these are the longest lived of all vertebrates.

Seasonal variations of environmental temperature do not affect greatly the thermal constancy of the milieu intérieur in most warm-blooded vertebrates. The temperature factor has less effect on

very low metabolic rate almost at the

Rance river where food is abundant, the growth is very rapid and the limpets reach a very big size, but die when two-and-a-half years old. On the other hand those living on exposed rocks along the coast, when water is less rich in organic material, have a very slow growth, reach a smaller size but live much longer (up to sixteen years).

Vertebrates

The prolonged life span of most vertebrates does not favour an experimental approach to the supposed correlation between the rates of energy-turnover and ageing We must rely on available information patiently gathered by ecologists and field-naturalists. *It is not usually possible with such data to attain standards of* precision comparable to well controlled laboratory studies. But they nevertheless give us some insight on the way the environment can differently influence the life-span of various populations of the same species.

position can be made in most cases On the other hand some species have a rather wide geographical distribution and live in waters whose temperature and food-content varies greatly.

In such conditions striking differences in growth rate, tempo of life and

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ife.

On the contrary the arctic subspecies found in Great Bear Lake (*Thymallus signifer signifer*) does not reach its sexual maturity before

reach their maturity ... (*Clupea pilchardus*) have a sl ... lower (1935) live longer in the En ... de Luz and Vigo.

Age determination in wild amphibians and reptiles being less reliable than in fishes, and in most cases quite impossible, the data on these two classes of vertebrates are scanty. Oliver (1955) has nevertheless given us recently some very interesting information on north American species.

The duration of the larval period of some widely distributed

life-cycle in the two cases is altogether different.

Among lizards striking latitudinal differences in growth-pattern

environment for two years. This warm climate norm to the

the northern race of the

fore necessary to infer
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in another.

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Seasonal variations of environmental temperature do not affect greatly the thermal constancy of the milieu intérieur in most warm-blooded vertebrates. The *temperature* factor has less effect on the energy metabolism of these animals than, for instance,

but continues throughout life; it is significant to find that these mammals which have a poor thermoregulat... rate of metabol...

October 1938 ...urlière 1947). More recently Dorst (1954) reported cases of marked *Rhinolophus ferrum-equinum* and M... reached respective ... longevities of 8 to ... is appears that in these mammals a reduced energy-metabolism and a low fecundity is definitely associated with a long life-span. Inversely, shrews, with their very high metabolic rate and fecundity are among the shortest lived mammals.

A very similar state of affairs seems to exist in some birds like swifts, hummingbirds and nightjars.

Such are the facts which suggest at the present some kind of correlation between rates of energy-turnover and ageing. Since the work of Rubner (1908) and Pearl (1928) our knowledge has slowly progressed and the influence on ageing processes of such factors as the "rate of living", the "tempo of life" and even the ... well find their comm... *on metabolic rate.* ... than a certain fixed ... and the rate of this energy-turnover appears to determine the rate *of ageing.*

If such a correlation is confirmed by more extensive experiments and observations it will remain to understand its underlying biochemical and biophysical causes. Some recent experiments showing that enzyme molecules have a definite life-span already suggest new approaches to that highly complex problem.

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o, 25, 67.

DISCUSSION

J. B. Hamilton. The studies of Dr. Clive McCay, as mentioned by Dr. Comfort, suggest that an irreversible form of ageing occurs upon maturation of rats, whether the animals have been starved previously or not. Somewhat similar findings have been reported in some invertebrates (Kopec, 1924) but not in all (Bishopp and Smith, 1938). This point deserves further study especially with reference to sexual nature protoplasmic re

R. L. Worrall. An animal's energy turnover building

demonstrated for a wide variety of tissues, ranging from the brains of bees to the muscles of men. The length of adult life, in man and other mammals, is thus a function of three variables:

1. The energy turnover.
2. The net loss of protein per unit of energy turnover.
3. The minimum amount of protein required for life.

With approximate numerical values for these variables in different animal species, the general factors determining the length of adult life can be handled mathematically.

[illegible]

1. The energy turnover.
2. The net gain of body protein per unit of energy turnover.
3. The maximum amount of body protein allowed by negative physiological feedback.

Each of the above variables is itself a function of others, the definition of which is a major task of biology.

THE AGEING OF MAMMALIAN CELLS

By

GEOFFREY H. BOURNE

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THE rates and the methods of ageing of mammalian cells appear to be different in various organs and tissues. Because of this fact Cowdry (1952) classified the cells of the body from the point of view of ageing as follows:—

1. Vegetat[illegible] little evidence of age change.

2. Differentiat[illegible] more keratin as they approach the surface.

3. Reverting post-mitotic [illegible] However, following injury, even in quite old animals they may rejuvenate in the sense that they undergo a series of rapid mitoses, and the relatively undifferentiated cells that result can differentiate into normally functioning cells of that organ. The cells of the liver, kidney, thyroid gland and salivary glands come into this category.

4. Fixed post-mitot[illegible]

protein) comes to an end because the synthetic capacity of the existing [illegible] ation of DNA however, fresh gro[illegible] has pointed out that a theory of [illegible] upon the exhaustion of *cell catalysts.*

Although cells of various tissues age in different ways and rates [illegible]

[illegible]

they are normally present in this condition, when the cells are taken from an old animal. Whether this is the result of increased *fragility in response to mechanical handling of the tissue or to the* fixatives used or whether they are in this state in the living cell cannot be stated with certainty. Furthermore, in old cells it is always more difficult to demonstrate mitochondria because there appears to be a [illegible]

[illegible] walls of blood [illegible]

[illegible] owls Payne has described changes in the mitochondria. At first they enlarge, then become vesicular. Many of them then fuse to form a single large body and at this stage the cell usually dies, the " chondrosphere " being liberated into the intercellular spaces. In the cells of the germinativum in ageing skin there is a reduction in the number of mitochondria Tissue culture cells, provided they are constantly [illegible]

[illegible] of cells is not unusual. If sub-culture is not carried out, however, degenerative changes followed by death occur. Characteristic amongst these are mitochondrial changes. These normally filamentous organelles break up into rods and granules or swell into small vesicles and there appears to be a nett decrease of mitochondrial substance. It may be significant that similar changes occur in [illegible]

[illegible] vessels. [illegible], at least [illegible] salivary [illegible] Andrew (1951).

These mitochondrial changes are of considerable significance. It is known *that something like 80 per cent of the enzymes of the Krebs*

cycle, which are responsible for the aerobic metabolism of the cell and which supply the energy required for oxidative phosphorylation, are found in these organelles; substantial alterations in their form and quantity must have a fundamental effect on the metabolic activities of the cell.

Fragmentation of the Golgi apparatus is also characteristic of degenerative tissue culture and aged tissue cells. For example, Sulkin and Kuntz (1952) have shown that in the ganglionic nerve cells of young dogs the Golgi material is composed of a loosely

[illegible]

material with the same staining reactions as the Golgi substance, but where it occurs it is in the form of discrete granules. It is likely that electron microscope studies will tell us a great deal more about the structural changes in both Golgi material and mitochondria in old age.

In degenerating tissue culture cells characteristic nuclear changes occur. The nucleus may divide without mitosis into two or more parts (Andrew (1955) claims to have seen evidence of amitotic division in the nuclei of the cells of the brain in old animals). Vesicles of nuclear sap may be squeezed out into the cytoplasm. In some cells the nuclear wall may break down and the whole nucleus may liquefy. In old nerve cells the nuclei may become pycnotic and show a decrease in nuclear histone which, according to some authors, suggests a diminished capacity on the part of the nucleus to synthesize nucleic acids In addition to pycnotic changes the nucleus may show an internal brushwork arrangement attached to one side of the nuclear membrane, and the nucleoli may show a honey-combed rim. Pycnotic nuclei have been described in many of the organs of old animals by a number of workers. Meyers and Charipper (1956) describe nuclear vesicles in the cortical cells of the adrenals of ageing hamsters.

In the cells of the autonomic ganglia of old dogs there seems to be a loss of chromidial substance (Sulkin and K[illegible]
the form of a peripheral chr[illegible]
and displaced and the cells [illegible]
there is a shift in the nucleo-[illegible]
nucleus. It is of interest th[illegible]
more resistant to age chan[illegible] the features
characteristic of ageing autonomic ganglia.

Cell membranes appear to alter with old age; certainly their permeability alters and presumably this indicates some structural modification Not very much work has been carried out on the permeability of mammalian cells—Lansing's work (1947) on permeability of old cells was carried out with *Spirogyra*. It is of interest that he found that the [illegible]

same direction for all compounds, for example, old cells were more permeable to alcohol and less to urea. This may also be true of the cells of the gastric mucosa of old human beings, at least for alcohol. As long ago as 1917 Herzfeld and Klinger showed that there was an increase of protein at the surfaces of old cells and that this interfered with the normal free exchange across the membrane.

[illegible]

of old human tissues, e.g. brain, sclera, arteries and elastic tissue

[illegible]

is an increase of

his excess of iron

reached a maximum in the rat at about $1\frac{1}{2}$ years of age and thereafter it remained constant for the rest of the life of the animal (3–4 years) This increased iron content was found only in the cells of epithelial organs, not, for example, in muscle cells. The authors discussed whether this increase of iron was of special significance or whether it was dependent on the destruction of blood during the lifetime of the animal. They claimed that this increased iron was not due to haemosiderosis, pointing out that it occurred uniformly in organs in which haemosiderosis does not usually occur. The low values for iron in young animals and the high values for old animals were found to be constant If the deposition of iron was due to destruction of blood one would expect the deposition of iron to be continuous throughout life—whereas this is not so. The authors quote this evidence therefore as proof that the increase of cell iron up to $1\frac{1}{2}$ years of age must have some functional significance. They point out the remarkable constancy of their results; that the increase of cell iron at various ages is so regular that it is possible to tell the age of an animal by an iron estimation They believe that the extra iron accumulated by the cell probably forms a compound other than those already present in the cell. It is of interest that changes occur in the haemoglobin iron of old mammalian erythrocytes (Lemberg & Legge 1949). In fact the ageing of erythrocytes is said to be due fundamentally to exhaustion of the system which maintains haemoglobin iron in the ferrous condition. It might be thought that this was due to the absence of a nucleus from the erythrocyte, but the avian erythrocyte, which possesses a nucleus and which appears to be able to synthesize haemoglobin continuously while the cell is in circulation, has a shorter life than the mammalian erythrocyte.

[illegible]

cell. It is of interest that in vitamin E deficiency pigment occurs in many cells and some authors have thought that the so-called senility [illegible]

[illegible] plinia even in paraffin sections. It was subsequently shown that this pigment was acid-fast (Endicott and Lillie, 1944). It also fluoresces a greenish yellow with the longer wave-lengths of the ultra-violet. Only pigment which has these properties is entitled therefore to be called "ceroid".

Pigments of this type have been found in or around [illegible]

One would expect that as cells age there would be a decrease in the various enzyme systems present in them. The falling off of oxygen consumption recorded by various authors (see Shock and Yiengst, 1955) suggests that this might be [illegible]

Despite these findings, however, my own preliminary histochemical preparations of young and old animal tissues indicate a slightly increased succinic [illegible] suggesting t[illegible] activities o[illegible]

A further [illegible] reaction of [illegible]

seventeen different organs in young and old rats. *Preliminary* observations indicate not a decrease in these hydrolytic enzymes in the tissues of old animals but rather an increase. This is most marked in the cerebrum and cerebellum (particularly in the Purkinje cells), in the brush border of the duodenum, and in the seminal vesicles; it was present but less marked in organs such as the liver and kidney. *The substrates used for the phosphatases included* glycerophosphate, which presumably demonstrates what is colloquially called "alkaline phosphatase" (which is, in fact, a non-specific phosphomonoesterase), oestrone and cortisone phosphates, pyridoxal phosphate, carbamyl phosphate and ethanolamine phosphate. The enzymes which dephosphorylate these latter compounds although *having their optimum pH in the region of 8 or 9 appear to be quite* distinct from the non-specific "alkaline phosphatase". The histochemical preparations which are obtained from their use are quite different from those obtained with the latter.

So far as is known at present, oestrone and cortisone phosphates are not formed in the metabolic processes involved in the *in vivo* metabolism of these compounds, so *that the increased dephosphorylation* of them in older tissue may simply be an aspect of increase in general phosphorylytic activity in these tissues. On the other hand, of the remaining three, two (pyridoxal phosphate and carbamyl phosphate) are metabolically important substances, while the rôle of

distributed

ciated with

ie prosthetic

group of several, and possibly all, amino acid decarboxylases, carbamyl phosphate is an important intermediary in urea synthesis in the body—it acts as a carbamyl donor in a variety of enzymatic systems.

physiologically very important substances towards the latter. It may be argued, probably quite justifiably, that histochemical preparations are artefacts and what goes on in them bears little relation to

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appear to be microsomes and in which most of the hydrolytic enzymes appear to be concentrated. Among these enzymes were β-glucuronidase, acid phosphatase, cathepsin, ribonuclease and deoxyribonuclease, and the name given to these bodies was "lyso-

somes". In a lecture at University College during 1956 de Duve described these bodies colloquially as "suicide bags" and claimed that their unrestricted activity after death was the cause of tissue autolysis The increase in activity in these bodies in old tissues either by loss of inhibitory control or otherwise may help to explain the progressive inefficiency and degeneration of tissues as they age.

Cytolytic activity resulting from the activity of lysosomes may be responsible for the loss of neurones from the brain in older animals. [illegible]

Purkinje cells in senile tissues for every 41 in the young animal. [illegible]

following numbers of Purkinje cells per given area of cerebellum in men of different ages: 42 years, 823; 65 years, 691; 79 years, 500; 94 years, 462; 100 years, 445.

Sulkin and Weatherford (1955) have shown that in autonomic ganglia in old dogs there is a decrease in vitamin C (as demonstrated by the acetic silver nitrate technique), changes in the Golgi apparatus, and accumulation of pigment and substances positive to the periodic Schiff reaction They also showed that similar histochemical changes could be produced in [illegible] a vitamin C [illegible] vitamin C n[illegible] old age res[illegible] decrease of the efficiency of the enzyme systems synthesizing this vitamin. It also raises the question as to whether partial deficiency of this vitamin over a very long period of time in human beings might not play a part in the initiation or acceleration of tissue changes usually attributed to the process of ageing.

Although it has been suggested that increase in hydrolytic [illegible] activity in old age m[illegible] of the tissue degener[illegible] problem of the contr[illegible] number of organs d[illegible] and it is also know[illegible] enzyme activity and [illegible] (1953) showed red[illegible] kidney, liver and [illegible] muscle following adrenalectomy and castration, and Brandes and Bourne (1955) showed loss of acid phosphatase from the Golgi region of the mouse prostate following castration, and its return to that site following implantation of testosterone.

seventeen different organs in young and old rats. Preliminary observations indicate not a decrease in these hydrolytic enzymes in the tissues of old animals but rather an increase. This is most marked in the cerebrum and cerebellum (particularly in the Purkinje cells), in the brush border of the duodenum, and in the seminal vesicles; it was present but less marked in organs such as the liver and kidney. The substrates used for the phosphatases included [illegible]

[illegible] enzymes which dephosphorylate these latter compounds although [illegible] of 8 or 9 appear to be quite [illegible]". The histo- [illegible] r use are quite [illegible]

So far as is known at present, oestrone and cortisone phosphates are not formed in the metabolic processes involved in the *in vivo* metabolism of these compounds, so that the increased dephosphorylation of them in older tissue may simply be an aspect of increase in general phosphorylytic activity in these tissues. On the other hand, of the remaining three, two (pyridoxal phosphate and carbamyl [illegible]

phospholipid metabolism. Pyridoxal p[illegible] group of several, and possibly all, amino acid decarboxylases, car- [illegible] synthesis in the [illegible] ystems. [illegible] ated in old tissues may be of considerable significance, [illegible] ndicate a shift in the balance between synthesis and hydrolysis of these [illegible] the latter. It may [illegible] prepara- [illegible]

the biochemists work[illegible] they specialize, namely tissue homogenates, we find that they have recorded an increase in other types of hydrolytic enzymes in the tissues of older animals, namely β-glucuronidase (Byrbye and Kirk, 1956) and acid phosphatase (Zorzoli, 1955).

In this connection it is of interest that de Duve and his colleagues (1955) have described in cells of rat liver a series of bodies which appear to be microsomes and in which most of the hydrolytic enzymes appear to be concentrated. Among these enzymes were β-glucuronidase, acid phosphatase, cathepsin, ribonuclease and deoxyribonuclease, and the name given to these bodies was "lyso-

It is possible that some of the age changes in nerve cells might be reversed with hormonal or other stimulation but no hormones will be able to bring back to the brain the cells which have already been lost by the ageing process

If many of the ageing changes of tissue cells are due to failure of

... were a hypertrophy of the liver, heart and spleen, that is the hypotrophic process of old age has been reversed. When thyroid hormone was used in addition to the anterior pituitary hormones there was a beneficial effect on all the organs studied

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Many papers in the literature have demonstrated the relations between morphological and biochemical changes in tissue cells and steroid and other hormones. In senescent humans and animals it

general increase of connective tissue in pituitary, adrenals and thyroid, in the pituitary she found an increase of basophil and chromophobe cells, in the thyroid loss of colloid or poor quality colloid and reduction in the size of cells. In the adrenal accumulation of what appears to be ceroid pigment and degenerative changes in the cells were found. A number of authors have studied the changes in these three endocrines in a variety of animals (see Blumenthal 1955) and degenerative changes in the reproductive glands are also well known and frequently recorded.

It may be, therefore, that tissue changes in age are due to progressive degeneration of the endocrine glands. Korenchevsky and his co-workers have shown that multi-hormone preparations can retard or reverse some but not all of the weight changes in organs due to age, and in some cases they aggravate the senescence changes.

Other workers have also studied the response of old tissue cells to hormones—Shock (1956) for example says that in tissues in old individuals which remain functional the response to steroid hormones judged by the N, K, P and Ca balances is the same as in the young subjects. Another investigation in this field was that of Masters (1953) who records the effects of sex hormone treatment of female patients who were over 60 years of age and who were all at least ten years past the menopause. These patients were followed until eleven of them died and autopsy material was obtained from the reproductive organs. The uterus and cervix were found to be increased in size and to be comparable in this respect with the normal for women between 20 and 40 years of age. The vagina was returned to a state identical in appearance with that seen in the fully functional vagina and reactivation of the cells of the breast was also obtained. Although microscopical section showed a reactivation of the blood vessels in the ovary the latter did not show a con-

tween
They
pointed out that the capacity for growth in epiphyseal cartilage declines with age and eventually ceases completely. On the other hand articular cartilage remains able to proliferate. Thus articular cartilage at any given age is in a younger state physiologically speaking than the epiphyseal cartilage. The latter has in fact

Apart from this however,

because cell division finishes while the leaf is tiny and the development of successive leaves is mainly just cell expansion. During this expansion

F. Digby. We are at a very early stage in the study of

outward symptoms

G. H. Bourne. I have no comment.

R. J. Ludford Several references have been made during this conference to the significance of mitosis in the ageing of *organisms*. Dr. Comfort suggested that one determinant of

The results of tissue culture work suggest that cells

continuous self-duplication. Aberrations of mitosis are frequent, and result in irregular distribution of chromosomes

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DISCUSSION

...

G. H. Bourne. That is an interesting experiment which would be well worth doing.

N. W. Pirie. The importance of distinguishing between the age of a cell and the age of a tissue is well illustrated by the tobacco plant. The cells in most of the leaves of a plant a foot high are of comparable age

SOME ENDOCRINE ASPECTS OF AGEING

By

G. I. M. Swyer

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Ageing is not unnaturally linked with the idea of rejuvenation, and rejuvenation with the sex glands, since loss of gonadal function may be one of the more outstanding general characteristics of ageing. It is of course many years now since the idea was first mooted of bringing about rejuvenation by means of gonadal extracts, trans-

it may be of some value to review the impact of ageing on the activity of these endocrine glands.

The gonads

Both the ovary and the testis have two distinct functions; to

proved necessary in order to explain certain facts of testicular physiology and pathology). In the testis, androgen secretion is

[illegible]

were degenerate.

Cytoplasmic structure undergoes a series of changes during mitosis, which is most obvious in differentiated cells in which the mitochondria and Golgi apparatus are confined to certain regions of the interphase [illegible]

[illegible] their original form and [illegible] Golgi apparatus is recon- [illegible] isible changes, there are [illegible]

[illegible]

It must, however, be emphasized that postmenopausal women do not generally show evidence of extreme oestrogen deprivation (such as may be found, for example, in Simmonds' disease, the pan- [illegible] of all the endocrine glands). [illegible] the adrenal [illegible] he latter may

[illegible]

intelligible explanation of the loss of function with increasing age, [illegible]

[illegible] to enjoy normal coitus, persists unimpaired in many postmenopausal women Clearly the endocrine aspect of sexual ageing in women may be quite independent of the psychic aspect. [illegible] somewhat different

[illegible]

many authentic examples of men in the eighties producing fertile semen and begetting offspring. Nevertheless, the testis does show evidence of ageing, though it appears to partake of the more general degenerative process which affects the rest of the body rather than of the quite specific process occurring in the ovary.

The decline in excretion of 17-ketosteroids with increasing age, to which more detailed reference will be made later, points to decreasing activity of the Leydig cells Actual observations of these in testis sections do not show any obvious decrease in numbers in [illegible]

age.

Doubts have been entertained regarding the existence of a male climacteric, but it may safely be accepted that there is indeed such [illegible]

tion of males do undergo a phase of waning testicular function and

Engel, 1947 and by del Castillo, Trabucco and de la Balze, 1947)
In the ...

... transformations which follow this and produce the corpus luteum.

Furthermore, oögenesis and spermatogenesis show fundamental differences in so far as the former appears to be a wholly foetal process while the latter occurs only in sexually mature males. The actual production of oöcytes takes place in the foetal ovary, under what stimulus is not known, and at birth the ovaries together contain something between 200,000 and 400,000 oöcytes. A substantial proportion of these are destroyed by atresia between birth and puberty. Thereafter, once menstrual function has become established, during each cycle one (or ...
and are expelled from the ovar...
destruction of some 20–30 other...
associated with them undergoing abortive development during the follicular or proliferative phase of the cycle, and atresia during the progestational phase when the ripe follicle has become a corpus luteum. In this way, there is a continual loss of follicles until eventually the stage is reached when few or none remain. Perhaps 400 will have produced eggs, and nearly a thousand times as many will have served the purpose, not of producing gametes but of secreting oestrogens, since there is little doubt that it is from the follicles developing during the follicular phase (as well as from the corpus luteum, and perhaps from follicles undergoing atresia) that ovarian oestrogens are derived. When all the follicles have been used up, it is clear that the ovary is no longer able to secrete oestrogen—or at any rate, not in the way it was formerly able to do so. It is this physiologically-determined ovarian insufficiency which is responsible for the cessation, either gradual or abrupt, of menstrual cycles which constitutes the climacteric.

After the menopause the ...

... conceived oestrogen therapy for climacteric symptoms. The anterior lobe of the pituitary gland is also fully effective and, because the decreased production of ovarian oestrogens has reduced their inhibitory effect upon it, increased secretion of pituitary trophic hormones, especially gonadotrophins, is the consequence. The thyrotrophic and adrenocorticotrophic hormones find responsive target organs and, so it is supposed, these glands may become more or less hyperactive. It is to the combination of lowered oestrogen levels and altered thyroid and adrenocortical function that the symptoms commonly experienced by climacteric women are usually ascribed.

of both.

The ratio of androgens to oestrogens is higher for men than for women at all decades until the ninth.

The output of neutral reducing lipids, which reflects the production of corticosteroids, is on the average higher for men than for women at all ages, and varies but little with age In contrast, the non-ketonic steroids, a mixture of substances of doubtful origin, part

steroids decrease much less markedly with increasing age in both sexes. The 11-oxyetiocholanolones decrease least of all; these substances derive chiefly from hydrocortisone and its metabolites

Steroidogenesis and ageing. The outstanding fact, referred to above, is that with advancing age the urinary output of corticosteroids changes very little while that of 11-deoxy-17-ketosteroids

may in consequence experience symptoms of the same general

female, usually between the ages of 55 and 65. The first to produce scientific evidence indicating the existence of a male climacteric were Heller and Myers (1944) who found that whereas in 15 men with psychoneuroses or psychogenic impotence the urinary gonadotrophin excretion was normal, in 23 men whom they considered to be suffering from the male climacteric the titre was unequivocably higher. Moreover, testicular biopsies on 8 of these men revealed a reduction in the size and activity of the seminiferous tubules, together with a reduction in the size and number of the Leydig cells, in 5 cases; and in the remaining 3 hyaline degeneration of the

histological characteristics.

According to Howard *et al.* (1950), the climacteric can be divided into a compensated and a decompensated stage. In the former there is a tendency to decreased production of gonadal hormones, which is met by over-production of pituitary gonadotrophin so that gonadal function remains essentially intact. In the decompensated stage, this tendency to gonadal failure is not counterbalanced, in spite of increased gonadotrophin, and so gonadal failure becomes clinically demonstrable. In the female, the compensated stage lasts only a very short time, but in the male, on the other hand, it is the decompensated stage which is seldom encountered. They therefore considered their patients with the male climacteric whose testicular biopsies appeared normal, in spite of increased gonadotrophin titres, still to be in the compensated stage.

The adrenal glands: changes in steroid metabolism in ageing men and women

The most deta
ageing men and
measured the
steroids, reducing neutral lipids (for corticosteroids), androgens and oestrogens in a group of 297 men and 320 women, all considered to be normal and healthy. It is possible only to summarize their findings here.

Oestrogens. In men, the output of oestrogens remains relatively constant with increasing age; in women, on the other hand, the output declines between the ages of 40 and 60 years, reaching a level somewhat below that of men, and thereafter remaining constant. Of the separate oestrogen fractions, oestrone and oestradiol

result of which the ratio of androsterone to etiocholanolone derived from the reduction of testosterone is increased, or, as a further possibility, that there is increased conversion of etiocholanolone to etiocholanolone-3α, 17β-diol.

An exercise test demonstrated a significant improvement in muscular strength in 10 of the men, which was maintained to a lesser degree for at least four and a half months after discontinuation of the treatment. On the other hand, there was no change in the psychological status, neuromuscular co-ordination or encephalograms of the subjects—nor were there any untoward effects.

effects of ageing.

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1955

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DISCUSSION

J B Hamilton The studies by Pincus and his associates extend and confirm much previous work by other

chromatographic

one another and

decreases markedly. This decrease is most probably due to a decline in the secretion of precursor hormones. Now the principal source of neutral steroid hormones appears to be cholesterol, and the two main pathways of its conversion are: (1) splitting of the side chain at carbon 20, leading to the production of Δ^5-pregnenolone, which is the prime precursor of the C-21 steroids; this process is stimulated by ACTH (adrenocorticotrophic hormone), whereas the subsequent reactions by which Δ^5-pregnenolone is converted into hormonal end-products occur independently of ACTH, as do those of the minor pathway to C-21 steroids which does not involve cholesterol; and (2) splitting of the side-chain at carbon 17, leading to the production of dehydroepiandrosterone, which is the prime precursor of the C-19 steroids; it is not known whether there is any pituitary trophic influence on dehydroepiandrosterone production. The fact that corticosteroid production is well maintained with advancing years may be taken to imply that the reactions involving breakdown of cholesterol to Δ^5-pregnenolone, as well as all of the enzymatic reactions leading to the conversion of the latter to hydrocortisone, remain unimpaired. The decline in androgen synthesis implies that the ageing adrenal cortex becomes less able to effect rupture of the cholesterol side chain at carbon 17, since this is the initial step in the production of the C-19 steroids of which the androgens form a part.

Studies of the steroid excretion patterns of ageing individuals given steroid supplements indicate that the capacity to convert these hormonal steroids to characteristic metabolites remains essentially unchanged. This is confirmatory of the hypothesis that the alterations in steroid output with age are primarily due to changes in steroid production and not in the subsequent metabolism of these hormones—with certain reservations mentioned below.

In their most recent report, Pincus and his colleagues (Freeman *et al.*, 1956) made investigations on a group of 14 men, aged 70 to 91, who received daily for five months a steroid mixture composed of testosterone, adrenosterone, hydrocortisone acetate and corticosterone in amounts which, on the basis of previous calculations, were expected to bring up the average level of blood steroids to those found in young men aged 20 to 40. This treatment had no effect upon the serum and urinary concentrations of inorganic ions, upon the blood eosinophil count or upon the excretion of creatinine. The total 17-ketosteroid excretion rose from an average of 4·5 to 17·1 mg. per 24 hours, was maintained at this level throughout treatment, and declined to pre-treatment levels on cessation of therapy. Although the excretion of 11-oxygenated steroids agreed well with the theoretical values, that of 11-deoxy-17-ketosteroids differed from

DEMOGRAPHIC ASPECTS OF AGEING

By

B. BENJAMIN

General Register Office, London, W.C.2

THE title of this paper can be regarded as ...

... retirement age.

A few simple facts may put matters in perspective:

(1) As yet (an important reservation) the increase in the pro-portion of elderly ...

(2) In the first half of this century ...

... of 65 year-old men surviving to their 70th birthday increased only slightly ... cent. The ... 0·80 years ... of course, ...

The ageing of populations

It will be advantageous to consider first the changes in the age structure of the population that have taken place in recent decades, since these changes have given rise to social and economic problems which have impressed themselves on the public conscience to the extent of exciting interest in the welfare of the elderly person as an individual. It is doubtful whether there would be the same interest that there is to-day in the process of ageing or ... the problem ...

... covering a comparison of mortality in England and Wales in 1950–52 with that in 1901–10.

something over fifty surgically-produced healthy eunuchs, 19 to 70 year of age, and in a comparable series of intact men. There was no evidence of compensatory increase in adrenocortical function after gonadect so that these subjects appear to p plicated by testicular secretions. which in man are chiefly metaboli significantly with age in either castr for 17-ketosteroid

Changes in fertility

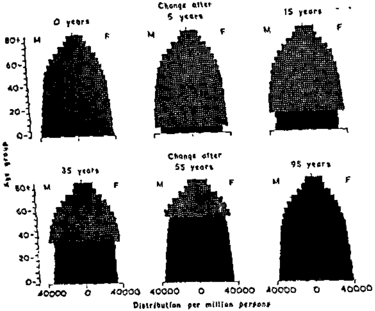

Fig 2.—Change in pyramid following fall in births

the base of the ...

... Eventually when the pyramid is wholly based on the changed birth intake its original shape is restored This is important, viz., that the effect on age structure of a decline in births is immediate; ageing is prolonged but the change is nevertheless not permanent.

Changes in mortality

A change in mortality will increase the size of those ... which deaths are ...

The population pyramid

It is useful to illustrate the age structure of a population by means of a pyramid (see fig. 1) in which numbers in successive age groups are represented by the areas of horizontal strips placed on top of each other with the youngest at the base and the oldest at the top (each strip is split into left and righthand portions proportionate to the numbers in each sex.) They form a pyramid because as a result

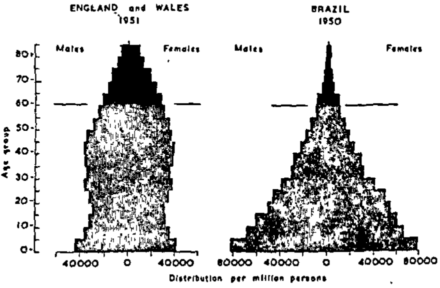

FIG 1.—Population Pyramids

of deaths the numbers remaining in successive age groups become smaller and smaller until a point is reached at which there are no survivors and this is the peak of the pyramid

The proportion of older people in the population, say those aged 60 and over, is represented by the part of the total area of the pyramid which is at the top above the strip which begins at age 60 (dark hatching of fig. 1). In a country with very heavy mortality

generations, the youngest or most recent being at the bottom.

It will be seen that up to the decade 1901–1910 births were increasing in numbers. The pyramid was broadening at its base (fig. 4). The reverse process of fig. 2 was taking place. The population structure was becoming youthful. In 1911 a stable population

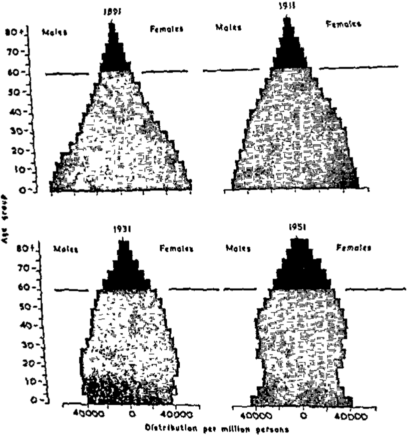

FIG 4.—England and Wales. Actual population pyramids, 1891–1951

sustained by constant births and subject to constant mortality—a "normal" population—would have had 10·4 per cent of persons aged 65 and over. The proportion was actually 5·2 per cent. Thus when the fall in births began to take place, the population was abnormally young and even if births had remained constant it would have had to "grow up".

reduction is only at younger ages this will increase the slope of the sides of the lower part of the pyramid but will not affect the top until sufficient time has elapsed for the increased survivors at younger ages to reach the older age groups. Fig. 3 shows the shape of a

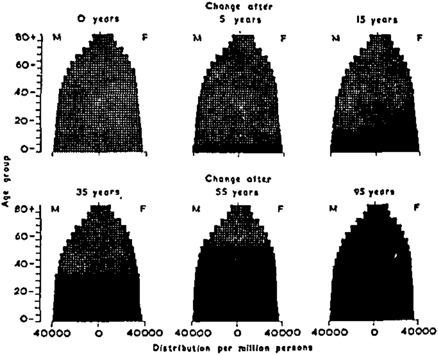

FIG. 3.—Change in pyramid following fall in mortality

typical pyramid 5, 15, 35, 55 and 95 years after a 50 per cent reduc- ... It will ... though ...

The actual changes in England and Wales

The changes that have been taking place in the age structure of the population of England and Wales have been in fact a mixture of the kinds of changes depicted in figs. 2 and 3.

Live births in England and Wales in successive decades from 1841 were:

1841–1850	5,488,736	1891–1900	9,155,153
1851–1860	6,471,650	1901–1910	9,298,209
1861–1870	7,500,096	1911–1920	8,096,222
1871–1880	8,588,782	1921–1930	7,129,070
1881–1890	8,890,238	1931–1940	6,064,516

Up to the present therefore the total fertility changes have made a much greater contribution to the increase in the proportion of older people in the population, than has the decline in mortality.

The ultimate effect of the changes

According to the most recent projection based on the

over.

There will be some changes at younger ages, though these will be comparatively small. Over the next twenty years the population

and in 1975 and 1995 the percentages are

population has "grown up" and has attained comparative stability in its age structure.

Dependency and economic activity

Older persons who have retired from employment have always consumed goods and services, whether purchased by their savings, by relatives or

An increase in numbers which is new but it does great importance in rel

This process of "growing up" was accentuated by the decline in births. The base of the pyramid became narrower and narrower, and a bulge was created which has now moved up to the higher age groups (fig. 4). If births remain relatively constant the bulge will cease to have any appreciable effect on the proportion of older people in the population by the end of the present century.

Side by side with these changes mortality has been steadily declining especially at younger ages at which the conquest of infectious disease has been most effective.

At most ages there have been considerable reductions in mortality since 1910. At younger ages there has been an acceleration in the improvement in survival rates in the last twenty or thirty years. The effect of this reduction in mortality has been to increase the steepness of the sides of the population pyramid up to quite advanced ages, i.e. to make it run up to a point less rapidly than it would otherwise have done. The full effect of this change will not be felt until those generations which have experienced the [illegible] century (*after* the effect of the past decline in fertility has largely disappeared).

It appears therefore that the temporary ageing of the population structure caused by fertility changes has only just reached its full extent and has not yet spent itself while the permanent ageing due to mortality improvement has yet to make its full impact.

It may be estimated that if mortality had remained constant at the level of 1910–12 the proportion of the population aged 65 and over at 1951, in England and Wales, would have been 9·7 per cent, compared with an actual proportion of 11·0 per cent. If annual births had remained constant at the level of 1901–10 the population in 1951 would have numbered 51·5 millions (instead of an actual population of 43·8) of which 9·4 per cent would have been aged 65 and over. On the other hand we have already seen that the 1911 population structure was already abnormally youthful as a result of earlier high fertility; this means that even if *both* mortality and fertility had remained unchanged the proportion aged 65 or more would have increased from 5·2 to 8·1 per cent in 1951.

We may set out these changes as follows:

Per cent 65 and over in 1911	5·2
Increase due to abnormal structure in 1911 (i.e. due to the prior rise in births)	+2·9
Increase due to fall in births since 1911	+1·6
Increase due to fall in deaths since 1911	+1·3
Per cent 65 and over in 1951	11·0

equated, a point on which it is difficult to give a clear answer. In 1995 children and unoccupied women will be fewer and workers [illegible]

future depend.

The ageing of individuals

There are difficulties in the way of extending the working life. Although mortality has been considerably reduced—to the extent that the expectations of life at age 65 on the England and Wales mortality [illegible] 11·3 an[illegible] vitality [illegible] death [illegible] of improved medical care does not imply the arrest of the relentless process of degeneration though doubtless raised standards of health have generally retarded this process.

[illegible] Wales during [illegible] ill be seen that mortality is increasing quite steeply even before age 60 and that after that age the rise [illegible] at 60–64 Further statistics supplied by the Ministry of Pensions and National Insurance show that the proportion of the insured male population who were sick on 5th June, 1954, and had been sick for more than three months rose from 1·73 per cent at ages 45–49 to 2·73 per cent at ages 50–54, and at individual higher ages the percentages were:

55–	4·33	60–	6·64
56–	4·61	61–	7·88
57–	5·30	62–	8·81
58–	5·48	63–	10·22
59–	6·51		

Subject to some reservations we may consider as elements of the dependent section of the population (1) children under age 15 (2) non-gainfully occupied housewives, etc. (3) persons who have attained the minimum retirement ages (for National Insurance purposes) of 65 (men) or 60 (women). The balance may be regarded as the supporting section ... proposed to estimate the ... in 1975 and 1995 by takin... –59.

We then obtain the figures shown in the table below.

TABLE I.—The economic pressure of the dependent population in England and Wales, 1901–1955 (numbers in thousands).

Year	Total population all ages	Children under 14 (up to 1931) 15 (1951–)	Non-gainfully occupied females 14–59 up to (1931) 15–59 (1951–)	Pensionable class i.e. males 65+ females 60+	Remainder	Ratio to (6) of Col. (3)	Col. (4)	Col. (5)	Total of cols 3, 4 and 5
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
1901	32528	9878	6565	1998	14087	·70	·47	·14	1·31
1921	37887	9772	8188	2972	16955	·58	·48	·18	1·24
1931	39952	8909	8521	3842	18680	·48	·46	·21	1·15
1951	43745	9733	8376	5990	19646	·50	·43	·30	1·23
1975[1]	46364	9219	8149	8462	20534	·45	·40	·41	1·26
1995[1]	46328	8885	8106	8742	20595	·43	·39	·42	1·24

[1] Based on the population projection referred to on p. 59.

Several interesting feat...

require the same relative amount of food and services as an adult) while the dependency of adult women has been a stable element.

equated, a point on which it is difficult to give a clear answer. In 1995 children and unoccupied women will be fewer and workers slightly more numerous, on the assumption of the population projection. The *total* national dependency will not be much greater in 1995 than in 1951.

[illegible] future depend.

The ageing of individuals

There are difficulties in the way of extending the working life. [illegible] duced—to the extent [illegible] England and Wales [illegible] 15·0; compared with 11·3 and 13·1 in 1930–32—it is not easy to interpret this increased vitality in terms of increased capacity to work. Postponement of death in an elderly person by improved medical care does not imply the arrest of the relentless process of degeneration though doubtless raised standards of health have generally retarded this process.

We are brought face to face with the [illegible] Wales during [illegible] ill be seen that [illegible] is increasing quite steeply even before age 60 and that after that age [illegible] These figures provide no [illegible]

T[illegible] Government Actuary on the National Insurance Act 1946 (1956) indicates that weeks of sickness benefit per annum per employed male in 1949–52 rose from 1·64 at 40–44 to 2·97 at 50–54, 4·17 at 55–59 and 6·11 at 60–64. Further statistics supplied by the Ministry of Pensions and National Insurance show that the *proportion of the insured* male population who were sick on 5th June, 1954, and had been sick for more than three months rose from 1·73 per cent at ages 45–49 to 2·73 per cent at ages 50–54, and at individual higher ages the percentages were:

55–	4·33	60–	6.64
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58–	5·48	63–	10·22
59–	6·51		

Subject to some reservations we may consider as elements of the dependent section of the population (1) children under age 15 (2) non-gainfully occupied housewives, etc. (3) persons who have attained the minimum retirement ages (for National Insurance purposes) of 65 (men) or 60 (women). The balance may be regarded as the supporting section of the population. It is proposed to estimate the non-gainfully occupied housewives, etc., in 1975 and 1995 by taking 60 per cent of the female population 15–59.

We then obtain the figures shown in the table below.

TABLE I.—The economic pressure of the dependent population in England and Wales, 1901–1955 (numbers in thousands).

Year	*Total population all ages*	*Children under* 14 (*up to* 1931) 15 (1951–)	*Non-gainfully occupied females* 14–59 *up to* (1931) 15–59 (1951–)	*Pensionable class i.e. males* 65+ *females* 60+	*Remainder*	*Ratio to* (6) *of*			
						Col. (3)	*Col* (4)	*Col.* (5)	*Total of cols* 3, 4 *and* 5
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
1901	32528	9878	6565	1998	14087	·70	·47	·14	1·31
1921	37887	9772	8188	2972	16955	·58	·48	·18	1·24
1931	39952	8909	8521	3842	18680	·48	·46	·21	1·15
1951	43745	9733	8376	5990	19646	·50	·43	·30	1·23
1975[1]	46364	9219	8149	8462	20534	·45	·40	·41	1·26
1995[1]	46328	8885	8106	8742	20595	·43	·39	·42	1·24

[1] Based on the population projection referred to on p. 59.

[illegible]

require the same relative amount of food and services as an adult) while the dependency of adult women has been a stable element. For the future it appears that pensioner dependency will in the next forty years rise by some 40 per cent but almost all of this rise will be offset by a fall in the dependency of children and unoccupied women in so far as the two kinds of dependency are capable of being

[illegible]

Clearly the problem of invalidity at ages even younger than the [illegible]

hardier members will face a growing burden of chronic invalidity arising from the sheer growth in numbers of older persons outstripping the slower improvement in their average vitality.

On the other hand surveys of the aged population have indicated that infirmity is more quickly developed and more passively accepted in conditions of stagnation and boredom and is more effectively resisted and prevented by interest and occupation.

The extent of employment

[illegible] of [illegible] we [illegible] be[illegible] Ce[illegible] the effect of National Insurance was to impose a virtually compulsory retirement age of 65 upon a large proportion of workers, the proportions of men gainfully occupied at older ages were as follows:

Age	*Per cent of males at each age, gainfully occupied*
55–59	95·0
60–64	87·5
65–69	47·2
70–74	27·4
75 and over	12·6

At the 1921 Census when there was some economic depression but no widespread system of contributory pensions to influence

60 and even before

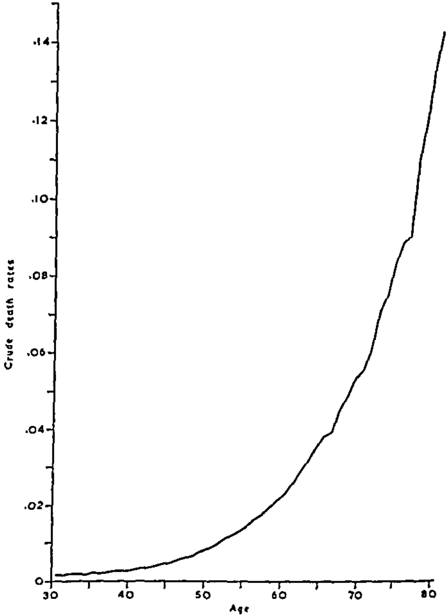

FIG. 5 —Crude death rates for England and Wales, 1950-52 males

The proportion begins to rise rapidly after age 60 and even before age 65 more than one-tenth of insured men are in poor enough shape to have been on sickness benefit for more than three months.

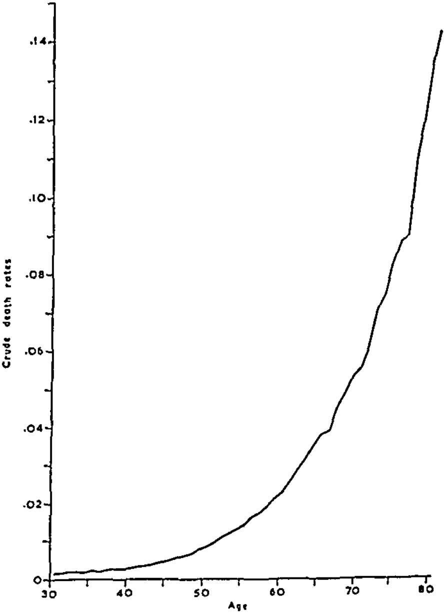

FIG. 5.—Crude death rates for England and Wales, 1950–52 males

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Practitioners' Records

Government Actuary. 1956 National Insurance Act, 1946, 5th Interim Report, HC 274.

DISCUSSION

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As a further example of a man being retired

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B Benjamin There is a case for saying that old people should have the opportunity to consider their own "merits"; taking medical advice but not having it imposed upon them.

N. W. Pirie. Is the increase in the proportion of women who get married a consequence of a change in the sex ratio or of the progressive removal of the disabilities from which married women have suffered in jobs such as teaching or the civil service?

retirement the proportions employed beyond age 65 were considerably larger, viz.:—

55–59	94·0
60–64	88·7
65–69	79·4
70–74	52·6
75 and over	27·0

Whether this is evidence of the sustaining [illegible] or whether it merely represents the [illegible] time working through stages of unfit[illegible] before contributory pensions were [illegible] difficult to judge. The real problem which the statistics do not at present measure is the extent to which the economy of the country fails to match the limited and specialized aptitudes of older workers to equally limited and specialized occupations so that they may make the maximum possible contribution to the national product within their physical capacity and enjoy doing it. There is a great need for really scientific and objective information about aptitudes—to this the family doctors may hold the key.

Housing and family life

There is one last demographic aspect of an ageing population which cannot be left out of account, viz., the family units in which older people live, especially in relation to the incidence of loneliness, and their housing conditions Tabulations of the 1951 Census (One per cent Sample) show that in Great Britain in that year there were 2,198 thousand households with married heads age 60 and over[1] and about half of these households, 1,129 thousand, consisted of two persons mostly but not quite all of them married couples living alone. Of 3,558 thousand unmarried[2] persons enumerated over the age of 60 about one-quarter, viz., some 904 thousand were living alone. There were also some 625 thousand unmarried heads aged 60 and over of households of only two persons. Finally account must be taken of a considerable number of unmarried persons aged 60 and over enumerated in non-private households, i.e. in hospitals, nursing homes, mental institutions, homes for the aged or infirm, and in larger hotels and boarding [illegible] containing at least 10 rooms); these [illegible]

The present picture [illegible] [illegible] institutions and hotels. [illegible] they seem likely to grow larger.

[1] Ninety-seven per cent of all married males aged 60 and over were enumerated in the status of head (or spouse of head of) of household.

[2] Single, widowed and divorced.

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DISCUSSION

R A M. Case. I should like to raise a point of terminology The

B. Benjamin The National Life Table for 1950–52 is under construction by the Government

N. W. Pirie If a medical board is considered competent to judge whether a scientist is fit to take

he directs. in the staff of the institute that

B Benjamin There is a case for saying that old people should have the opportunity to consider their own "merits"; taking medical advice but not having it imposed upon them.

N. W. Pirie. Is the increase in the
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B. Benjamin. It is difficult [illegible] has improved the marriage prospects of younger women but it is also clear from the persistence of high marriage rates that these prospects are being taken advantage of more readily and at younger ages by both sexes.

P. Townsend. The two ideas of "dependency" and "support" in old age are fundamental to discussion of the economic "burden" of old age. In Table I Dr. Benjamin shows past and future trends in the economic pressure of the dependent population. As dependents he includes children of school or under school age, non-gainfully occupied females and people of pensionable age. The question of the dependent population is a tricky and important subject. In the first place, future population estimates are continually being revised. During the War for example Beve[illegible] population in the 1980s which was [illegible] estimates for the same years, and [illegible] the economic problem of the aged has been conducted on the assumption that a decreasing number of [illegible]

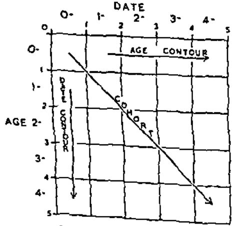
example, has decreased by a million, and presumably many housewives have taken over the same work, yet why call the latter dependents and not the former? There are many other difficulties in sorting out what one means by the "dependent" population. The housewife *supports* her husband so that he can go to work. What I am saying is that most workers are supported by dependents. Old people often support their relatives as much as do young wives their husbands. In an investigation carried out in East London recently two-thirds of grandmothers over the age of 60 were found to have the regular care of at least one grandchild. The grandmother helps her married daughters and sons living in neighbouring streets just as they help her. In the last twenty years in Britain there has been an increase of over a million in the number of married women at work. I believe this increase is related to the increase in the number of grandmothers in the population. The upshot is we need to be careful about our statements of the changing number of dependents in the population and how far old people depend on or support others.

B. Benjamin. I quite agree with Mr. Townsend. The statement in my [illegible]

Committee on the Economic and Financial Problems of Provision for Old Age" (1954. Cmd. 9333, H.M.S.O.)

the whole population

Reference has been made elsewhere to the greater survival rate of women but I believe that the general impression is correct that though women last longer they seem to age more completely while they are doing so.



THE PRINCIPLE OF ANALYSIS BY COHORT AND CONTOUR

Fig 6

(i.e. date) and the other in equal intervals of time added to the starting age of the animal. If for simplicity we assume the starting age to be zero also, this axis will be age.

It is now obvious that observations relating to the original batch of animals will fall along a diagonal (marked "cohort") of this grid. If

is kept under different environmental conditions, we should not regard the record found in a vertical column as a biological statement of the mortality experience of the type of animals used, since each successive

measures available to them at each age In other words, they were a batch of animals kept under different conditions.

England and Wales in the last century when viewed by cohort. (The figures are drawn from a quinary-quinquennial grouping and the cohorts labelled with the central birth-date of the group contributing to the life-experience described). In order not to overload the figure, cohorts spaced twenty years apart have been selected The progressive improvement in mortality experience is shown, and it is now clear that to extrapolate these curves, which is what must be done to obtain an expectation of life from this method, would be nothing but guessing.

I should like to make it clear that I do not claim that one statistical

accounting.

Miss E. A. M. Bradford In considering the supposed financial burden of the aged it is well to remember that, as time goes on, with the contributory pensions system people will, in effect, be paying their own

Pensions, as now arranged, are not a charity to the aged given by a benevolent population but a convenient means of compulsory saving for those who cannot, or will not, save during their best financial period of life.

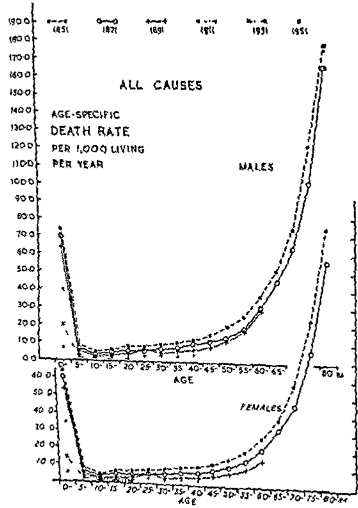

1851
1871
1891
1911
1931
1951
ALL CAUSES
AGE-SPECIFIC
DEATH RATE
PER 1,000 LIVING
PER YEAR
MALES
AGE
FEMALES
AGE

Fig 7

FUNCTIONAL CHANGES WITH AGE IN RELATION TO THE EMPLOYMENT OF THE ELDERLY

By

W. Hobson

Department of Social and Industrial Medicine, Sheffield University

... case of women and sixty-five in the case of men. But the onset of ...

Whilst it may be difficult to define old age as far as the individual is concerned, it is sometimes easier to define ageing in relation to the ...

... in general there tends to be cellular atrophy, fatty infiltration and increased pigmentation. There is an increase in connective tissue and a decrease in tissue elasticity, particularly in the skin and blood vessels Bones tend to become decalcified and calcium to be deposited in other situations, such as arteries, thyroid, pleura, cartilage, tooth pulp, valves of the heart and scar tissue. These changes may be partly due to a ...

whilst ...
by a ...
variati ... pulse have a much greater significance in the elderly. There appears to be a wide range in the resting pulse

... in the special senses are very important in determining ... higher tones, ... men.

hand, is more common ... arteriosclerosis of the labyrinth. This can be most distressing, leading to falls and fractures, and is an important cause of impaired mobility (Droller and Pemberton, 1953) Visual acuity and the ... the minimum amount

accuracy, that in the great majority of people physiological senescence in the human lens is reached at the age of fifty years, but it begins before puberty

Until recent years, we have had little information on the normal ranges of many of the biochemical variables, and even the values for younger age-groups are often based on inadequate figures. Thus serum cholesterol, serum alkaline phosphatase and blood urea levels are all higher than in younger age groups.

Physical Capacity

full of snags and do not necessarily apply to conditions as found in occupational situations It is well known that after maturity, the speed reaction time and strength of skeletal neuromuscular mechanisms are decreased In moderately hard physical work there is very ... older persons, apart ... evere work, however, ... with age; the chief

rate, and in a pers... pulse rate of 74 ... degree of tachycardia. Symptoms a... less conspicuous than in younger persons and minor deviations take on a greater significance. Repair is much slower and there is a narrower margin ... much more detrim... is anaemia is

The rise in b... becomes pathological. It it is much mor... known, but is clear that many old people can remain perfectly healthy with a raised blood pressure. Hobson and Pemberton (1955) found, for example, that in a random sample of old people living at home, 43 per cent had a resting diastolic blood pressure of 100 millimetres of mercury or over and the majority of these were in good health.

In the central nervous system there are a number of changes which, although in a younger person they would be of clinical significance, appear to be of little importance in the elderly. Thus, muscular weakness, brisk knee jerks, wasting pupils which do not react to light, and loss of vibration sense, can all occur in the absence of any evidence of organic disease. Similarly, there are certain mental changes which are characteristic of old age, such as impaired memory for recent events, which may make it difficult to take an accurate history. Apathy and depression have important effects on behaviour.

There can be little doubt that an adequate well-balanced diet is an important factor in preserving the health of the elderly. Mental factors characteristic of the elderly such as apathy and forgetfulness may adversely influence health by leading to a monotonous and inadequate diet. In addition, atrophic change... tract which can have ma... for instance, achlorh... over the age of sixty ...), and the concentration of pe... ...ptic activity fall off markedly in later life (Meyer, Spier and Neuwelt, 1940). Recent surveys have established the high incidence of chronic atrophic gastritis over the age of fifty years. It is well known that dyspepsia and constipation are common. These various factors are no doubt responsible for some of the wasting or malnutrition that occurs in old age, or, in severe cases, for deficiency diseases such as scurvy and anaemia.

Changes in the skeletal system can have an enormous effect upon person's physical capacity although they might be quite un- nportant as a danger to life. Examples of these are arthritis and efects of the feet, both very common. Rheumatoid arthritis, for ample, limits greatly the skilled work that can be performed by e hands and is a great disability to a musician or typist or to the usewife. Osteoarthritis and spondylitis of the spine are both very ppling deformities for a labourer. The tendency to decalcification particular danger when falls occur.

... out some experiments of a rather

...

entrance and administered again thirty years later showed that scores are on the whole higher on the re-test.

It would appear that although many age changes are continuous

...

seventy.

There is a great need for further research in this field and we require more information on the actual occupational capacity of different age-groups. The selective process which weeds out the more unfit with increasing age, complicates studies in this field and indicates a need for longitudinal follow-up studies of groups of individuals in younger age-groups.

Chronic Sickness in Old Age

...

... a high percentage, at least

and are more marked. There is a similar decrease in dexterity. Older men who have had mechanical training appear to be able to maintain the speed rates of young adults (Miles, 1954). This lends experimental proof to the well-known observation that experience and practice can counteract the increasing disabilities of old age. Smith (1938) made a study of men of different age-groups working under conditions similar to those found in factories and he confirmed the observations of Robinson that in short periods, or with moderate work, the performance of the elderly was comparable to those of the younger age-groups. When, however, the conditions became arduous, there was a definite decrease in the ability to perform high-speed manual work. In all age-groups, however, there are great variations in individual ability, so that some of the older workers were able to better the performance of some of the younger workers. This is an important consideration and emphasizes the principle that individual differences should be taken into account whenever the capacity of elderly persons is being considered.

Especially important in old persons is accident proneness. De Silva (1938) found that many of the components involved in the driving of a car showed a steady deterioration over the age of thirty years but the mileage driven per fatality showed an improvement with increasing age, at any rate up to the age of fifty years Vernon, Bedford and Warner (1928, 1931), in their studies on the accident rate in coal miners, found a decrease in frequency up to the age of fifty years and that increasing care and experience can counteract the decreasing performance which might be predicted on the basis of physiological factors alone. The figures for absenteeism are of interest in this respect but the results as one would expect are conflicting since they are biased by the fact that only those able to maintain good attendance records remain employed

Intellectual Changes with Age

A considerable amount of work has been carried out on the relation between intelligence and age and changes are found similar to those noted in sensory and motor efficiency, particularly where speed is concerned. This decrease in the score achieved in the intelligence test takes place near the age of fifty years. Again there are wide individual differences in every age-group. The smoothed curves indicating the decrease with age in intelligence test scores take the form of a parabola, with a rapid rise up to the age of fifteen years, reaching a peak about the age of twenty years, and a gradual fall after the age of fifty years, with a more rapid decline after the age of seventy years

The ability to learn depends largely upon the intelligence, so that memory function, ability to learn new tasks and tasks involving the relinquishing of old habits are found to be more difficult for old

" One thing is certain; ry broadest generaliza- ns are so very diverse ıch in their capabilities, search in

advising on the employment of the elderly.

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DISCUSSION

T. Levitt. I was very intrigued to note the high values attained for cholesterol in normal men (409 mg. per cent) and normal women (481 mg. per cent) The values for alkaline phosphatase were similarly high (up

W Hobson The survey was carried out on a random sample of old people over pensionable age living at home, either alone or with spouse Everyone showed some evidence of disease; I consider that any person who did not at this age should be classed as being decidedly abnormal We excluded any cases which were suffering from a disease which was a recognized cause of alterations in the serum cholesterol or alkaline

one-third, of all over 65 suffer from impaired physical capacity as a result of chronic disease.

Age and Retirement

The evidence would seem to lend no support to the idea of fixing sixty-five years of age for retirement from employment rather than, say, seventy. In view of the wide variations in abilities found in the older age-groups it might be thought desirable to have some means [illegible] person from continuing work after the age of sixty-five years, for example, severe angina, a previous stroke or failure of vision. It is important to remember that those with the best educational and cultural background show the least change with age and any diminution in the powers of critical reasoning may be more than compensated by the knowledge and wisdom gained as a result of experience. One thing is certain, and that is that there is a great need for more refined tests which will measure intellectual capacity in the aged. The present tests do not measure many of the higher mental abilities and tend to discriminate against the elderly, particularly where speed is a factor. They take no account of difficulties due to physical disabilities, for example, deafness, tinnitus, defects of vision, tremor, weakness

Although prior to the war the percentage of elderly workers in whole-time employment was falling, it would appear that this trend has now been halted; at any rate in 1954 there were employed in this country, 870,000 men and women over pensionable age and 230,000 over the age of seventy years. Fleming (1955), in a survey [illegible] power than others.

[illegible] l worker. The [illegible] seventy years, [illegible] tly raised the [illegible] r higher educa- [illegible] ge of 706 years have been brought out of retirement in order to undertake teaching. [illegible] years of age.

According to Fleming, what is required is, ". . . an approach which includes one or several of such industrial procedures as a periodic medical check-up of such persons, job analysis and work study applied in this connection, later-age counselling or retraining, or

work if its health and general conformation allowed; or it might be disposed of for relatively light work on a farm. I am informed that a Corporation horse or a goods horse on the railways employed on heavier work but at a slower pace might, after having been acquired at six years, enjoy an average working life of a further eleven years or more.

It is impossible, however, to discuss the subject in brief, because much would depend on the hours and conditions of work. When men become legally entitled to work shorter hours, so usually do their horses; and the working lives of horses may then be prolonged by the resulting avoidance of colic, undue fatigue and strained tendons. The market value of a horse is ...

...formance as a draught animal. Among horses that survive the hazards of injury, disease and ... ...pectation of life from b... ...f twenty-five to thirty y... ...of its reported working life seems to merit some research...

With regard to the working lives of timber-hauling elephants, Departmental Instructions for Forest Officers in Burma (1936) state that for purposes of valuation mature animals would be reckoned as those from 21 ...

elep...
55th...

...in the forests. But wastage due to disease, accident or overwork would evidently ... have been ...

...sufficient ... and in ... says that it may cause the forearms to lose their great development of muscle and the legs to become thin.

shown by younger subjects for heavy work, heat, humidity, long hours, etc. The evidence from these sources may or may not be relevant if we happen to be dealing with ageing subjects who have been for many years exposed to the same conditions. It would be more profitable to examine patiently what factors are applicable to ageing subjects, possibly indeed to ageing subjects alone. In other words, we need a type of job analysis that takes account of the physical and psychological changes we suspect to be characteristic of advancing years. But we have one great advantage. The tasks carried out by an ageing man or animal are usually " constant " in the sense that they have probably been on the same jobs for most of their working lives. Any decline in their effectiveness or staying power is thus measurable or it can at least be described in objective terms. The results of a study of this kind have always to be reduced to a statistical form, because the tasks undertaken are so varied and the characteristics of ageing differ so widely from one subject to another. If we carry our investigations far enough, certain common patterns and common factors should begin to emerge. Though all research of this kind is necessarily laborious, our consolation is that we may discover ways of easing and possibly prolonging the useful working lives of innumerable elderly men; and this would often be of far greater moment to the men themselves than the mere knowledge of an approaching dissolution.

I am more especially interested in the human problem, not only because I am human but because it seems to me that we have reached a stage in our affairs at which all records of the working lives of draught animals are going to become progressively less available to us. Industrial and agricultural undertakings that may formerly have kept reliable records are replacing horses with tractors and motor vans; the old records have often been long since destroyed, and annual redundancies among horses are making current records, such as they are, virtually useless for estimating the average working life. The literature of the horse is curiously lacking in statistical information on the subject of ageing. For the most part we have to rely on the memories of experienced men. The range of ages up to which a horse may continue on the work for which he had originally been bred or acquired is naturally a fairly wide one; but an age of 10–15 years is commonly stated to be the average. Ensminger (1951) says that " the market value of the animal increases rather sharply with maturity and then decreases beyond eight years of age. On the other hand, for many purposes horses are quite useful up to twelve years of age or even longer " It appears that in London the railway yards would normally have been acquiring horses at about six years of age; and the medium-built trotting horse used in the light parcel vans would then have been expected to remain on the job for an average of six further years or maybe less. It might then be transferred to slower and possibly heavier

of men aged 60–64 in various large occupational groups who recorded on their census forms that they were by that age already in retirement, ran as follows:

TABLE I.—Percentages of Men aged 60–64 who had already retired from the Occupations in which they are Classified.

Occupation	*Percentage already in retirement*
Building Workers: (Bricklayers, Plasterers, Labourers, etc.)	5·0
Painters	6·2
Farm Workers	6·7
Textile Workers	6·8
Plumbers	7·1
Workers in Wood: (Cabinet Makers, Carpenters, etc.)	7·8
Dockers	7·9
Coal Miners	10·1

Though Census figures of this type have to be handled cautiously, it seems probable that most of the men who here said they were in retirement had in fact left work

Williams (1953) records the occasional use of "old crock elephants" (presumably those over 55 years or more) in pushing and lifting logs with the head, tusks and trunk from the sand banks of rivers into the main channel. This is described by him as "a form of work reserved for pensioned tuskers suffering from old age, deformities or incurable wounds that made them unfit for harness". As for the final cause of death in old age, Evans (1910) says that death may occur suddenly "from long-continued and unobserved disease of the heart. The heart on post-mortem is sometimes enormously enlarged and may rupture from extreme exertion". He adds that in old animals degeneration of the blood vessels may predispose to rupture, and that this may be brought about by violent or prolonged exertion. A further description given by Williams (1950) suggests that he considers deterioration of the heart a fairly normal cause of death in aged elephants. "His cheeks are sunken, his teeth worn out. Gathering his daily ration of 600 lbs of green fodder has become too great a tax on his energies, and he knows he is losing weight Old age and debility slowly overtake him"

In a personal letter Lieut.-Colonel J. H. Williams has written, "I would say that an elephant of 50 needed particular watching. He was placed in the company of younger animals, that could take the biggest strain, the longest haul and the heaviest timber . . . If he lost condition at all at that age, it was doubly difficult to put it on again. . . . The first sign of age really affecting the animal's work was loss of power in his legs. In other words, he looked as if he must sit down to work rather than stand. He gave the impression that, if his head and his trunk could be used without taxing his strength by climbing the mountain side, then he held his own. . . For this reason, at 60 years of age, generally speaking, the animal continued his work on the flat with his tusks, trunk and forehead. . . I have known many elephants that continued until they were 70, and they were mostly on that work from 60 to 70 years of age. Between 65 and 70 they often showed signs of giddiness, slightly staggering if kept long hours"

The ageing man in industry has naturally been more closely studied in recent years than have horses or elephants. But no attempt will here be made to review the literature of the subject. I shall confine myself to a few examples of research procedures that seem to be yielding good practical results.

To demonstrate briefly how the statistics of occupation, health and age may be combined for the purpose of research, I will ask what proportions of working men are likely to have become more or less incapacitated for further work by their mid-sixties. In most manual occupations men do not retire by choice before they reach the pensionable age of 65. Men have nevertheless to pass into retirement before that age if they are compelled to do so by injury or sickness. According to the 1951 Census (1 per cent sample), the percentages

A study of industrial records usually enables us to arrive at a provisional estimate of the rate of wastage in old age, provided the records have been kept with sufficient care. As an example of provisional estimates of this kind, I reproduce a table that was based on small samples of old building workers, bus drivers and bus conductors. The contrasts are suggestive of the significance of the job itself in determining at what comparative ages men have to leave their various occupations. The records were taken without bias from among the records of men who had recently left employment and were traceable to the last moment of service with the undertakings in which they had been employed. Some allowances were made as far as possible for the relatively few cases of men who had not been removed solely by reason of old age, sickness or death; but it must be adm[illegible]

[illegible] building workers in my sample were employed on maintenance and repairs; and they probably had a better average chance of surviving late on the job than they would have had under the more arduous conditions of constructional work.

TABLE II.—Rate of Industrial Survival as affected by Age, Ill health and Death.

Age	60	63	65	66	67	68	69	70
Building Workers (320) per cent still on job	100	89	83	75	63	55	46	32
Bus Drivers (150) per cent still on job	100	86	78	50	31	21	15	7
Bus Conductors (150) per cent still on job .	100	85	80	35	26	23	16	11

It must be noted, then that the [illegible]
all traced from the ti[illegible]
60. In each case the [illegible]
at that age apparentl[illegible]
successive years [illegible]
their occu[illegible]ions by [illegible]
fact the industrial s[illegible]
Whether those who [illegible]
[illegible] or retired from their customary jobs found some light alternative work, in most cases we

year, from the mid-fifties upwards, reaching a level of 8·9 per cent of all the men at risk at the age of 63[1].

While statistical evi[illegible]
retired before their [illegible]
several years earlier [illegible] chronic sickness, it seems yet certain that the ailments of old age increase steadily from the mid-fifties onwards. By the time they are due for a State pension, at least 10 per cent of the men may probably be reckoned as more or less beyond further work. It would not be [illegible]
estimate what [illegible]
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tear. [illegible]
work; [illegible] some concessions in the hours
worked or the part they play in a labouring gang or the[illegible]
seek transfers to some [illegible]
indubitably [illegible]
and research [illegible]
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workers on t[illegible] were able to continue to the
retiring age. On other operations [illegible]
to move to other [illegible]
health. Heavines[illegible]
tempo of work, di[illegible]

In other words, [illegible] of
the work that seems [illegible] Provided he is
given opportunities for adjusting the mode and timing of his work progressively to his age, there is probably little reason for supposing that an experienced healthy old labourer could not accommodate himself in comfort to most of the strains imposed by any heavy lifting, excavating, etc, he has to undertake But Belbin does not mention that the various hazards, emergencies and [illegible]
that a man may [illegible]

[1] It will be obse[illegible]
duration than [illegible]
paper "Demo[illegible]

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60. In each case th [illegible]
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successive years [illegible]
their occupations b [illegible]
fact the industrial [illegible]
Whether those wh [illegible]
customary jobs fou [illegible]
[illegible] alternative work, in most cases we

do not know; but a number of them certainly made an effort to obtain further employment.

The decline in numbers over the mid-sixties is not invariably, and perhaps not even largely, due to a tradition of retiring at 65 years. In several industries men seem to delay the moment when they go in search of a less arduous job until they have the security of a pension on which to fall back; and they incline thus to procrastinate in spite of increasing strain or disability. Cumulative evidence from a variety of sources suggests that in many occupations at least 20 per cent of the men are compelled by their mid-sixties to moderate or change their form of work if they are to have any prospect of remaining in settled employment. This 20 per cent lies over and above the 10 per cent of men who have probably by that age been forced through chronic ill health into final retirement. The proportion for whom concessions become unavoidable increases thereafter roughly with the ages of the men, though in some occupations (e.g. bus driving or work at a coal face) few allowances could be made for a man's age.

What I am suggesting, then, is that the working lives of animals and men offer us a chance of glimpsing, and even in some degree measuring by a reliable yardstick, the physical changes that indubitably characterize old age. Under favourable conditions of care and health working animals could provide us with the better subjects for study, because animals presumably have less regard for conventional ideas about old age and about the proper age of retirement. But, as I have said, we have possibly come too late in history to use draught horses and hauling elephants for research of this kind. The study of men under industrial conditions will involve us in Work Studies of a very special type, in which we shall have to distinguish what varied factors in the relation between the ageing men and their jobs are making it necessary for the men either to moderate or to change their form of work. We should have to avoid ready-made theories and presuppositions. The method of research recommends itself, because in our ignorance of what happens in senescence we should at least be observing men just as old age was undeniably overtaking them

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DISCUSSION

W. E. Kershaw. I and my colleagues have for some time been interested both in the longevity of parasites and of their insect vectors, and in the ... of a property which may be termed the "infective potential" of ...

... time proved to be of two types, some being normal and others log-normal in their distribution. We are at the moment unable to understand why this difference should occur and what its significance may be.

W. Wilson ... There are two remarks I should like to make ...

being developed all over India as asylums for cattle which have passed their accepted working life.

The second point arises from the discussion on the propriety of a fixed retiring age. While from the biological point of view there is much to be said against fixing a retiring age, any form of social insurance would appear to make such fixation essential. We are faced in the tea industry in India with the introduction of a social insurance system involving a statutory provident fund and retrenchment and retirement compensation but since it is at present virtually impossible to terminate any worker's employment, apart from senior executives, I find myself bound to support the fixation of a definite retirement age. While naturally biological factors must be taken into account, the reasons for fixation are not so much biological as financial and economic

PSYCHOLOGICAL CHANGES WITH AGE: THE PRESENT STATUS OF RESEARCH

By

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It is perhaps important to make it clear from the outset that the

perfectly understandable: there are a great many old people these days, most of whom are in need of care, of understanding, and of workable solutions to their difficulties. Nevertheless, here as elsewhere in the biological sciences pure and applied, it is likely that prevention will in the long run prove better than cure; if this be agreed, then it is the *process* we must study, rather than the end-product

As any organism develops, it changes; as man is a relatively complex organism, the changes will naturally be difficult to assess. More importantly, as the time-span within which these complex

available regarding the psychiatric and psychologic changes occurring with advanced age, little agreement exists as to what these changes are or what they mean" The purpose of the present review is to gather together some of the more satisfactory research material in such a way as to indicate points of departure for fresh enquiries.

Beach (1954) has suggested that three generalizations may be made about all aspects of organic development Of these the first two are sufficiently familiar to be amusing: "Development

is not constant, but rises to a maximum at a particular age and then decreases."

The outstanding feature of our present picture of the developmental process is certainly one of failing potentialities, and it might

be tempting to regard Beach's generalization as but a different way of saying just this. There is however the other aspect, allowed for by Beach, but not so often noticed in the general literature on ageing: a "decrease in sensitivity to environmental influence" may well represent a *psychological asset—but only if we are prepared* to regard man as more than an input-output system. The outstanding work of Lehman (1953) leaves us in little doubt that, so far as the creative intellectual fields of endeavour are concerned, both quality and quantity of output reach their peak early in life—in almost all fields before the age of 40. But he does note (p. 330) that "as a result of positive transfer the old usually possess greater wisdom and erudition. These are *invaluable assets." Wisdom may* well be the fruit of the contemplative years which lie beyond the point of "decreased sensitivity to environmental influences"—but by its very nature seems likely to prove resistant to objective measurement. This being the case, it is only natural that most of the quantitative findings so far presented in the literature, being of a kind dependent on continued interaction between the organism and the *environment, should tend to show varying degrees of decline with* age. On the available evidence from medical and physiological sources, Lehman (1953, p. 328) is probably justified in stating that "a decline occurs prior to 40 in physical vigour, energy and resistance to fatigue". Adverse changes with age are also characteristic of the two principal distance receptors—the eye and the ear. For practical purposes it would appear desirable to face the fact, however *unpalatable it may be emotionally, that in Lehman's words* "possibly every human behaviour has its period of prime". This done, it may be easier to see the objectives for psychological research on the process of ageing as being in the words of Bromley (1956b), "to point the way towards reduced stress and greater achievement during the mature and declining years". These are "applied objectives"; the approach to them must be made both by the direct *route and by the more circuitous path of relatively "pure"* enquiry.

Perception

Reference has already been made to the eye and the ear: lest their pre-eminence be questioned, we may do well to note the judg*ment of Sherrington, as quoted by Adrian (1949)*: "*The distance* receptors are the great inaugurators of reaction . . . (they) integrate the individual not merely because of the wide ramification of their arcs to the effector organs through the lower motor centres, they integrate especially because of their great connections in the high cerebral centres."

Loss of elasticity in the lens starts in childhood, resulting in a *gradual narrowing of the range of accommodation,* while acuity

for distant objects begins to show decline from about 45 years of age (Crouch, 19; 45 Dennis, 1953). Adequate knowledge of changes in the perception of depth and of colour is not yet available, but McFarland and Fisher (1955) have shown that complete dark

sound stimula "as reflected in decrease in mean maxima and minima pupil diameters, extent of constriction, and response velocity." After drawing attention to th...

... of this number many may be helped by surgery or by visual aids"

So far as hearing is concerned, it is well-established that there is a

... and not yet adequately understood; while it may be possible that the normal decremental process may be accelerated or its results made more severe by a sustained high-intensity noise in the working environment, it is known that a noisy background sometimes assists the older person to maintain an adequate communication level.

Finally, it is worth noting that no studies have yet been located in which *both* vision and hearing have been studied in the ... dividuals in relation ...
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[illegible]

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sound stimula "as reflected in decrease in mean maxima and minima pupil diameters, extent of constriction, and response velocity". After drawing attention to the need for studies of such variables as states of stress, tension and fatigue, and the effects of various drugs, she adds the positive note that "the older

cent have sufficient visual impairment to interfere with their activities . . . of this number many may be helped by surgery or by visual aids."

So far as hearing is concerned, it is well-established that there is a progressive hearing loss with age, principally however in the higher frequencies above 2,000 c p s. This results in problems of inter-personal

noise are not yet adequately understood: while it may be possible that the normal decremental process may be accelerated or its results made more severe by a sustained high-intensity noise in the working

Motor Performance

The development of muscular strength, according to Fisher and Birren (1947) " follows a systematic trend with an increase up to the late twenties and a decline, usually at an increasing rate, from that time on ". Simple reaction time in response to an auditory stimulus

tion has yet come to the notice of the writer. Apart from the apparent differences in experimental technique, and the fact that the proportionate increase for Birren and Botwinick's study is double that for Obrist's, the two investigations agree in providing evidence of a slowing down with age. Birren (1955) elsewhere quotes Rashevsky as his authority for stating that " in general, the stronger the peripheral stimulus, the shorter the reaction time ". The relation of this general observation to age might well repay close experimental examination.

Movement time was until recently also regarded as showing a marked increase with age, largely due to an early study by Miles (1931). However, from evidence presented by Leonard (1953), Szafran (1951) and Singleton (1954), consistent with the general findings of Rubin, von Trebra and Smith (1952), it seems clear that although there is some increase (mainly after 45–50 years of age) it is small in relation to that which has been demonstrated for decision making at the critical points in a psychomotor task. This leads us directly to the studies of skilled performance in relation to age

importance " so far as complex psychomotor skill is concerned.

or outgoing action ", and of the two latter it is the failure in " perceptual organization " of the incoming data which is the more serious probl connection with ion to the work xplain his results (obtained in two very satisfactory experiments on aiming) one must conclude " either that older persons are reluctant to rely on reduced sensory cues in the performance of a task, or that they need to marshal all possible sensory data in task performance ". As the latter suggestion itself provides an explanation for the former, it is logically to be preferred, and it is consistent with Welford's theoretical position. Welford himself mentions (1953) the findings of Weston (1949*a* and *b*) that " poor lighting, small size of detail to be

seen, and lack of contrast between objects viewed and their background can lower speed of work between the twenties and the fifties, even when subjects are matched for visual acuity by Snellen charts and Jaeger test types". Improvement in one or other of these respects would of course increase the available sensory data relevant to the task, and this would consequently benefit the older people relatively more than the younger. Welford makes the point (1953) that analogous results might be obtained in an auditory inspection task where a particular sound might be critical.

Adult Learning

It is of course but a short step from considerations of sensory and psychomotor efficiency to an examination of our present knowledge about adult learning in relation to age. There are, broadly speaking, five main aspects of this fundamental psychological topic: intellectual ability, short-term retention of new material, long-term remembering, problem-solving, and creative thinking. This is not of

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same subjects under timed and untimed con-

at 65 than at 50 years, it is not known whether a loss in memory ability during this period consists

of a small loss experienced by many, [illegible]
few." [illegible]
to the [illegible]
was only half as great.

The evidence concerning long-term remembering is conflicting, largely due to the almost complete absence of longitudinal studies of individuals and to reliance on material obtained from psychiatric subjects. Jones and Kaplan (1945) present a good deal of this conflicting material before coming to the conclusion that "since memory defects are frequently progressive, we are not justified in talking about senile memory as a single condition. The fact remains that memory defects are, perhaps, the most salient psychological symptoms of ageing, both normal and pathological." This seems rather strong for the available objective evidence.

So far as problem-solving is concerned, Clay (1954) has demonstrated that when time-stress is not present, the performance of older subjects (55+) compares well with that of younger subjects (<25) on a simple problem, but as the complexity of the problem is progressively increased, the older subjects become slower and less accurate, and finally in some cases fail to complete the task. Kay (1951) approached the study of problem-solving from an unusual angle by, in effect, giving his subjects the solution: their task was then to think how to make use of it. He says rightly that this technique "does give us some precision which is open to further analysis. By predicting certain types of mistake it is possible to confirm what it is that is holding up a subject's progress". This approach enabled Kay to combine the results obtained in this task with those from a rote-learning study, leading him to the conclusion that it was "reluctance to discard their own ideas which characterized a poor performance both in the learning and in (the problem-solving) experiment". The implications of this conclusion for the re-training of older workers must be obvious, and it also suggests the need for fresh examination of the oft-quoted "rigidity" of older people and the assumption that this is a "personality" feature of old age.

Further reference to creative thinking in the ordinary sense covered by the work of Lehman (already quoted) seems unnecessary, but attempts to tackle the problem directly by a planned study are so rare that a recent paper by Bromley (1956a) is most welcome. He used the Shaw Test, publicized by Howson (1948) and adapted by Bromley himself. It consists of four wooden blocks which can be arranged in different series, according to height, weight, position of a notch, and so on. Bromley concludes from the use of the test with 256 men and women, aged 17–82 years, that "although loss of intellectual efficiency with age does not entirely account for the decline in quantity and quality of creative output, it does account for the major part". His measure of "intellectual efficiency" is

having in large part the connotation of "productivity" in circumstances where the subject's responses are for all practical purposes not limited by the nature of the task. In view of the work of Howell (1955) previously cited, it would be of great interest to see to what extent variations in "creativity" or "productivity", as measured by the Shaw Test, can be accounted for in terms of the "hold" and "don't hold" groups of W-B sub-tests.

Emotional Stability

So far as it is possible to judge from the available literature, our

is clearly a great need here for sound research by relatively objective methods.

Work Performance

We come finally to a consideration of what is known about the effects c

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the original performance is maintained, but only by means of increased effort. Second, a change of method may enable achievement to be maintained or even improved.

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leaders, they found, feel older workers are capable workers and are also victimized by prejudices of their own about older workers. [illegible]

tion. Belbin (1955) however examined the commonly-held view that older people should be transferred to lighter work, and the implication that heavier work is not suited to older persons. He found that "those occupations which could be recognized as heavy and strenuous tended to have a higher proportion of persons engaged on them between the ages of 45 and 60 than did lighter skilled operations in the same industries".

Conclusion

[illegible] has been taken [illegible] That there is [illegible] be emphasized is that significant progress cannot be achieved without carefully-controlled longitudinal studies of individuals.

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DISCUSSION

F. Verzar I admired the excellent lecture of Dr. Heron and should like to underline two points which he raised.

First, the importance of experimental psychological studies of the ageing process. He pointed out that there are not only deteriorations but also some well-proved improvements in certain qualities in the aged.

The irreversible decrease of elasticity of tendons and skin, the loss of physical strength, etc , are parts of the basic changes in the tissues during life. Our main practical aim in gerontology is, I think, not rejuvenation in the common sense, or prolongation of life beyond its natural limits, but rather to keep the aged in such physical health that they can use what we may summarize as their experience for the benefit of the community. Loss of physical health reduces life expectancy, but increased experience coupled with relative health makes the old person a leader of his group. From such a point of view, experimental psychological research is not only of theoretical but also of the highest practical value. It may be able to show us, not merely in general but also in certain definite cases, such as the work of factory workers, medical men, scientific workers, teachers, etc., the particular type of work in which the older ind [illegible] 'd replace the younger to the advantage [illegible]

I fully agree also with the seco [illegible] Research on ageing should not [illegible] f different ages [illegible] Two years a [illegible] has started work [illegible] long term investigations on the same [illegible] workers from a particular factory, in which they usually work from early youth to old age, are examined individually systematically every one or two years by an ophthalmologist for changes leading to presbyopia, by a medical officer for general health, by a physiologist for pulse wave velocity, etc The first report was given in April 1956, by Dr R. Bruckner at the Basle Symposium on Experimental Research on Ageing. We very much hope that similar research will also be started by other research groups.

NUTRITION AND AGEING

By

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Introduction

clear that the concept of growth here adds anything other than confusion, and whereas becoming older implies mere passage of time, becoming old implies showing signs of old age An infant as it

of nutrition.

Nutrition before Maturity

Maturation is the process of coming to full growth or development, which state is called maturity. There are various criteria of maturity: maximum length, ability to reproduce and the menarche are the three commonest A fully-grown eunuch has reached maturity, a spawning fish has also reached maturity: therefore neither ability to reproduce nor maximum length can be taken as an *absolute* criterion

A great many experiments
before maturity delays
of these facts have bee
1903), for butterflies (
(Chapman, 1920), for
for *Daphnia* (Ingle, 1 and Banta, 1937), for caterpillars of *Lymantria dispar* (Kopec, 1924), for tadpoles (Kopec, 1928), for the limpet *Patella vulgata* (Fischer-Piette, 1939), for

[illegible] (McCay, Dilley and Crowell, [illegible]), for rats (Jackson, 1937; [illegible] 47; Riesen, Herbst, Walliker and Elvehjem, 1947; Templeton and Ershoff, 1949; Sherman, Campbell and Regan, 1949), and for cattle (Hansen and Steensberg, 1950). Northrup (1917) for example showed that undernourishment of *Drosophila* during the larval period prolonged this and increased duration of life from nineteen days to twenty-nine days. Kopec (1924) fed and starved caterpillars on alternate days, and thereby could prolong the duration of the larval stage from about 16 per cent to about 90 per cent of that of control animals, the [illegible]

(1952) showed that undernourishment of the sessile protozoan *Tokophrya infusionum* prolonged life whereas overnourishment shortened it. The most careful and extensive work has been done by McCay and his associates. For instance, in experiments started in 1930 (McCay, Sperling and Barnes, 1943; McCay, 1952) it was found that rats could be retarded as much as 1,150 days by undernourishment and still resume growth when adequately fed. They lived longer because of slower development of the chronic diseases that attacked the lungs, kidneys and middle ear, and tumours developed more slowly (as had been earlier shown in mice by Moreschi (1909)). McCay concluded that the type of aliments provided in an adequate basal diet mattered little in relation to life-span; the amount of aliments, or number of calories, was the important factor.

Is life [illegible] maturity [illegible] rate? Th[illegible] (1912) with tadpoles. The simple explanation that rapid growth shortens life does not seem to be correct: Carlson and Hoelzel (1946) found that intermittent fasting prolonged the life-span of rats and retarded the development of mammary tumours, but without influencing the growth rate. McCay's undernourished rats were active, and although their basal metabolic rate was somewhat lowered their total metabolism was normal. The evidence is against the effects being brought about through altered rate of development. The effect of undernourishment is probably mediated through the pituitary. We could suppose that food stimulates the anterior pituitary to produce both gonadotrophic hormone, so that development takes place, and growth hormone which allows phospholipids to be synthesized in the body with the aid of essential fatty acids. If these phospholipids are formed, growth occurs; if they are not formed, through absence of essential fatty acids or absence of growth hormone, growth of the body does not occur.

Since it is very consistently found amongst lower animals that overnourishment hastens maturity and shortens the life-span whereas undernourishment delays maturity and prolongs life, the same might be true of man. In 1832 Edmonds published his "new theory of the cause producing health and longevity". He believed that hardship in youth tended to decrease the rate of

quand, 1951) Conversely, undernourishment is known to delay

follow these children, of whom we have records, through life. Brody (1945) showed that the proportion of life-span used in reaching maturity is constant for higher animals

and now by medication with vitamin B_{12} and aureomycin, even though these activities make them grow more quickly and mature earlier" (Sinclair, 1951). Even earlier (Sinclair, 1948) I had tried to point out that "insufficient thought
desirable rate o
We can make
otherwise be by injecting anterior pituitary lobe extract; alternatively we can make him heavier and probably taller by superalimentation. There is indeed a tendency amongst nutritionists to regard the child of perfect nutriture as placid, rotund, red faced, and seated in contented contemplation of its folds of flesh. During the past several years there has been a marked increase in the rate of growth of children, although in England and the U S the adult male
has remained unchanged. *It*
in rate is necessarily advanta
since the long time taken to
human genus" This is a ve
cussed at the Ciba Symposiur
what lonely crusade has been *joined* by McCance (1953; McCance and Widdowson, 1955) It may be that we should consider as the best diet in regard to ailments that which

passing almost immediately into a long period of senility would be unfortunate. To some extent McCay's increased longevity was gained at the expense of the period of maturity before senility was apparent. The whole subject deserves more attention.

I have discussed aliments only because little is known about the effects that deficiency or excess of nutrients before maturity has upon senescence. For instance, Fritsch (1953) found that the amount of pantothenic acid in the medium was an important factor in determining the life-span of *Daphnia;* this and similar observations may complicate some of the results obtained with undernourishment. Lansing (1942) found that rotifers live longer in a medium low in calcium, and he suggests that senescence is caused by an increase in calcium at cell surfaces with lowered permeability and accumulation of toxic metabolites inside cells. Research in the field of nutrients is badly needed.

Nutrition after Maturity

Whereas most of our information about the effects that nutrition before maturity has upon senescence is derived from experiments upon lower animals, most of our information about the effects of nutrition after maturity is derived from observations upon man. There is good evidence that overnourishment after maturity increases the incidence of [illegible]

In lower animals the [illegible] undernourishment of the larv[illegible], undernourishment of the imago does not and may even decrease it (Kopek, 1928). However, adult ticks, *Dermacentor variabilis*, that have become attached to a host and are feeding freely, die within a few weeks, whereas unattached adults can live for more than two and a half years (Bishopp and Smith, 1938). McCay found that the effect of undernourishment upon life-span was much less in rats when it occurred after than when it occurred before maturity (McCay, Maynard, Sperling and Osgood, 1941).

It has been known from ancient times that fat men die earlier: *Plures crapula quam gladius* (Gluttony kills more than the sword). That careful observer Robert Burton may have come very near the truth when he wrote in the *Anatomy of Melancholy*: "As a lamp is choaked with a multitude of Oyl, or a little fire with overmuch wood quite extinguished; so is the natural heat with immoderate eating strangled in the body." Certain of those who had indulged immoderately in food and drink, such as Luigi Cornaro (1558) and the Miller of Essex, were driven to temperance by the dread of their former sufferings.

[illegible]

Dublin and Marks (1951) and Armstrong, Dublin, Wheatley and Marks (1951). Dublin analysed the mortality of persons who had been insured as sub-standard risks because of overweight between 1925 and 1934 and who were traced to 1950 It was high, and increased markedly with the degree of overweight. As I have pointed

relatively minor disorders that are more frequent in the obese mainly for mechanical reasons; degenerative arthritis in knees, hips and lumbar spine; fractures;

maximum at about the age of twenty-five years, and their decrease thereafter is certainly a criterion of senescence. It appears that appetite does not decrease as much as does muscular activity after this age, and of course there are usually

commoner in obese women and rarer in undernourished women

The most interesting and important of the disorders that are commoner in the obese are the

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In view

cardiov disease and its relation to nutrition, some discussion is required.

I have put forward elsewhere reasons for believing that a relative deficiency of the essential fatty *acids*, *linoleic* and arachidonic, is becoming increasingly prevalent in this country as in most other highly civilized countries (Sinclair, 1956a, c, d) These acids are of course easily destroyed by oxidation, by hydrogenation and even by

conjugation of the double bonds as by ultra-violet light. The "unnatural" (all-*trans* or *cis-trans*) isomers, and isomers with conjugated double bonds act in the body as antagonists of the ordinary required isomers which are all-*cis*. "Unnatural" is not an ideal term because cow's milk and butter contain almost none of the ordinary form of linoleic acid and a relatively large amount of *cis-trans* linoleic; cod-liver oil contains no ordinary linoleic acid. This may be yet another reason for thinking twice about pouring jugfuls of milk down the throats of children and spoonfuls of cod-liver oil down the throats of infants. Deficiency of essential fatty acids caused by consumption of diets low in them and containing the "unnatural" isomers produces disorders. High unsaturated fatty acids occur in the body in cholesteryl esters, in butyl alcohol, in glycerophosphatides (particularly ethanolamine phosphatide) and in cardiolipins (where linoleic acid represents five-sixths of the total fatty acids). These polyethenoid fatty acids include others besides linoleic: C_{20}— and C_{22}-polyethenoid acids occur abundantly in the glycerophosphatides of liver and brain (Klenk and Lindlar, 1955; Klenk and Dreike, 1955), and can be formed from linoleic in presence of vitamin B_6 (Witten and Holman, 1952) by addition of acetate followed by dehydrogenation (Steinberg, Slaton, Howton and Mead, 1956). This vitamin is not the only one that plays a part in their metabolism vitamin E protects them from oxidation. But much of the vitamin E in our diets is destroyed by the so-called flour improvers; and the content of vitamin B_6, formerly not high, has decreased considerably since the bread subsidy ended on September 30, 1956.

When the essential fatty acids are absent they may be replaced by oleic acid or saturated fatty acids synthesized in the body; this may also occur if there is a relative excess of saturated fatty acids as perhaps on diets high in aliments, or in diabetes mellitus in which large amounts of fat are metabolized. The essential fatty acids can also be replaced by unusual highly unsaturated fatty acids if these are present in relative excess. The unusual compounds so formed do not function properly in the body and therefore can give rise to degenerative disease. For instance, Dr. Basnayake and I found two years ago that rats on a fat-free diet esterified cholesteryl with fatty acids synthesized in the body rather than with highly unsaturated fatty acids which the body cannot form, and the unusual ester was deposited in the skin; similarly, serum phosphatides were raised and had an unusually low iodine number In coronary thrombosis the atheroma might be caused by deposition of an abnormal cholesteryl ester, and the increased coagulability of the blood might be caused by a raised concentration of ethanolamine phosphatide, which is known normally to contain an unusually unsaturated fatty acid and which Robinson and Poole (1956) have shown to increase the coagulability of blood.

There are two conditions in infants in which atheroma, commonly regarded as a sign of senescence, is said to occur: progeria and

sensitivity to vitamin D (Sinclair, 1956b); the adult form of this deficiency with adequate dietary calcium and vitamin D might be

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caused by defective membranes of the cells of the stratum granulosum. It is possible that the alteration in permeability of old cells might be related to imperfection of the lipoprotein polymer. In deficiency of essential fatty acids

accumulates in old cells is related to peroxide formation from unsaturated fatty acids. It would be interesting to study these changes in old cells in relation to essential fatty acids.

Effects of Senescence on Nutrition

Digestion and absorption become impaired in old age. Loss of teeth, diminished saliva, and diminished gastric acid contribute to this. Half a century ago Metchnikoff thought that senescence was caused by poisons derived from intestinal putrefaction, and heroic measures were taken in the interests of intestinal hygiene; now we venerate our intest

effi xygen are less

im cells may be

Requirements may be altered. The increase in body-fat and decrease in muscle that occur with ageing raise two important questions: first, what is the "normal" amount of fat and what represents obesity in the elderly? secondly, should the calorie requirements be decreased? From the work of Shock it seems

eating, and this increase is undesirable. There is a conflict of opinion about calcium requirements of the elderly: osteoporosis is probably more related to failure of protein anabolism than to dietary calcium deficiency.

The most important effects of senescence upon nutrition are those *associated with conditions that are all too often found in old persons:* poverty, ignorance and apathy.

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DISCUSSION

G. P. L. Miles. I do not presume to argue with Dr. Sinclair on the ...

A. Piney. Among the chemical accompaniments ... ageing, there ar...

[illegible]

eating, and this increase is undesirable. There is a conflict of opinion about calcium requirements of the elderly: osteoporosis is probably more related to failure of protein anabolism than to dietary calcium deficiency.

The most important effects of senescence upon nutrition are those associated with conditions that are all too often found in old persons: poverty, ignorance and apathy.

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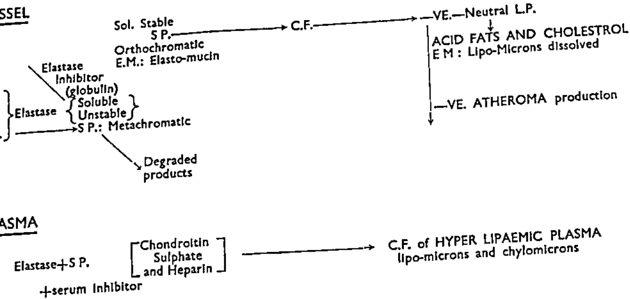
Diagram showing a proposed Mechanism for the formation of an Anti-Lipaemic Factor

...Elastin; C. Collagen; G.S., Ground Substance; S.P., Sulphated Polysaccharides; C.F., Clearing Factor, L.P., Lipoprotein; Sol., Soluble; —ve, Negative.



enough is already known to indicate that, even if they do not start the degenerative atherosclerotic process, they contribute to its progress.

Over the last forty years, many attempts have been made to incriminate one or more single fatty constituents of the serum. Thus, it has been supposed that a high level of blood cholesterol can lead to atheroma; certainly feeding experiments in rabbits suggest that this is the case. Others have incriminated the lipids in general, and so on.

My own observations strongly suggest that deposition of the fatty materials in the walls of arteries is facilitated, or perhaps even directly caused, by disproportion of the main fatty substances in the blood. Normally, the ratio between cholesterol and phospholipids is 1:1, but, in association with active atherosclerosis, this lipolytic quotient is usually raised but may be lowered. Some shift of the quotient seems to be a part [illegible] lipolytic quotient to revert to normal, and by reducing the abnormally high beta fraction of the lipo-proteins. It seems to follow that research [illegible] lecithin-fraction from soya beans, together with other surface-active agents, but already it is possible to assert that, in most cases, the pathologically altered lipid-spectrum reverts to normal or nearly normal.

Miss H. Saxl. Recent research carried out at the University of Leeds by the Nuffield Gerontological Research Unit indicates that an antilipaemic factor is formed in tissues which are rich in mucopolysaccharides such as the connective tissues of the vascular system, the liver and the blood, by the interaction of the pancreatic enzyme elastase with certain components of the serum. The following mechanism has been suggested for the reaction and is shown on the diagram.

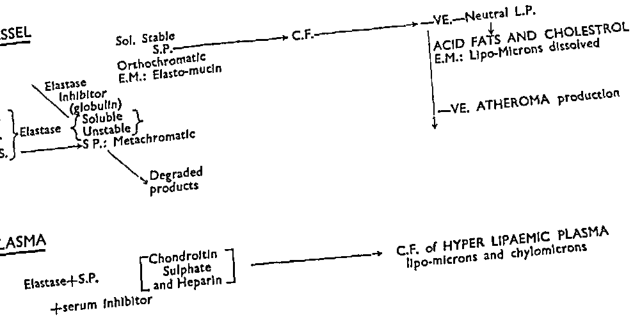
A. In the presence of elastase and especially the fraction which has elastomucase activity, the mucopolysaccharides are made soluble and unstable.

B. The serum inhibitor for the enzyme elastase is related to the α-globulin fraction. Its action is to control the enzyme in the formation of degradation products. This was estimated as a proteolytic function with biochemical methods and it also inhibits the removal of the soluble polysaccharides and makes them stable. Histological studies indicate that metachromatic substances become orthochromatic and that an absorption complex of the orthochromatic and elastica staining substances occurs which has the appearance of an amorphous elastin under the electron microscope.

[illegible]

DIAGRAM SHOWING A PROPOSED MECHANISM FOR THE FORMATION OF AN ANTI-LIPAEMIC FACTOR

Elastin; C. Collagen; G S, Ground Substance; S P, Sulphated Polysaccharides; C F, Clearing Factor; L.P., Lipoprotein; Sol., Soluble; —ve, Negative.



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My own observations strongly suggest that deposition of the fatty materials in the walls of arteries is facilitated, or perhaps even directly caused, by disproportion of the main fatty substances in the blood. Normally, the ratio between cholesterol and phospholipids is 1 : 1, but, in association with active atherosclerosis, this lipolytic quotient is usually raised but may be lowered. Some shift of the quotient seems to be a part of the ageing process, so that the idea that atheroma itself is an ineluctable consequence of innumerable microtraumata throughout life is not wholly acceptable. Furthermore, there is now a good deal of evidence that the rate of deposition in the arterial walls can be slowed by causing the lipolytic quotient to revert to normal, and by reducing the abnormally [illegible]

Miss H. Saxl. Recent research carried out at the University of Leeds by the Nuffield Gerontological Research Unit indicates that an anti-lipaemic factor is formed in tissues which are rich in mucopolysaccharides such as the *connective tissues of the vascular system*, the liver and the [illegible] of the pancreatic enzyme elastase with certain [illegible]

A. In the presence of elastase and especially the fraction which has *elastomucase activity*, the mucopolysaccharides are made soluble and unstable.

B The serum inhibitor for the enzyme elastase is related to the [illegible] to control the enzyme in the formation [illegible] stances occurs which has the appearance of an amorphous elastin under *the electron microscope.*

C. As a result of the above interaction, a lipase is activated. Biochemical investigations indicate that the quantity of inhibition is directly [illegible] to the amount of lipolysis. The lipase degrades neutral [illegible]

[illegible] on the lipids of vascular tissue [illegible] factor".

H. M. Sinclair. The effect of the introduction of electrocardiograms was allowed for in the study on coronary thrombosis

The classical discovery of Anitschkow, who produced a lesion simulating human atherosclerosis by feeding rabbits with cholesterol, has resulted in an intensive effort over the last twenty years to link atherosclerosis to a faulty lipid metabolism. Anitschkow observed that if the ingestion of cholesterol was discontinued after the feeding had been carried out for 3–4 months, a resorption of lipid occurred in the inner layers of the arterial wall, although the characteristic lipid plaque remained in the media for a much longer time.

Studies of the localization of the enzyme action point to the fact that the high concentration of polysaccharides in the inner layers of the vascular wall, together with an elastomucase, protects these against the deposition of the lipid. This would explain the observations of Anitschkow that the lipid was absorbed from the intima of the arterial wall after the cessation of the cholesterol feeding

G. C. Kennedy. I wonder if it is too inconoclastic to question the significance that has been attached to these " classic " papers of McCay's that Dr. Sinclair and several other speakers have mentioned. It is true, is it not, that McCay had to make several attempts before he could get the [illegible] did not seem to be a cause of death, and the incidence was unaffected by [illegible] breakdown occurs quite rapidly even in young rats, and is accompanied by loss of weight, staring fur and a general appearance such as is shown in McCay's pictures of " old " rats. I think it is simply the appearance of the chronic uraemic rat.

E. Digby. I doubt whether the effects of under- and over-nourishment are always as stated. There is much under-nourishment in India and China but the general impression is that both maturation and puberty are earlier there than in Western Europe.

G. H. Bourne. The answer to Mr. Digby is that maturity does not occur earlier in Eastern countries.

G. I. M. Swyer. There is no evidence that Indian women are nubile at an earlier age than Europeans.

F. Le Gros Clark. I know of no real racial differences in the maturation of human beings. There is some evidence that in Belgium, wartime under-nourishment led to a delay in the onset of puberty.

GENETIC VARIATIONS IN AGEING

By

J. MAYNARD SMITH

Department of Zoology, University College, London, W.C. 1

THERE are two kinds of differences between individuals which can

is strictly relevant to the problem of ageing, because in neither case does the susceptibility of an individual to the factor causing death increase with age.

The study of ageing is concerned with those changes in individuals with age which render them more liable to succumb to one or more

genetically homogeneous population of the fruitfly, *Drosophila subobscura*, kept in mated pairs at 25°C, and transferred to fresh food every second day. In no case is it possible to state the cause

age it was exposed to them.

Figure 1 also shows that life span is, in this and most other populations, a continuously varying character. Individuals do not fall into two or a few sharply defined classes. Such characters

ever the danger in this procedure that maternal age itself may influence the longevity of the offspring In parthenogenetically reproducing rotifers, Lansing (1948) showed that lines maintained from the eggs laid by young mothers could be kept indefinitely, whereas if the later eggs laid by a female were used, there was a progressive decline in mean life span in successive generations, and

For these reasons, there is less information on the genetics of ageing than of many other quantitative characters. However, what information there is is of some interest. I shall describe first some experiments on laboratory populations of *Drosophila*, and then consider how far these agree with observations on human populations.

parents, which suggests that crossing unrelated animals may give

be deleterious. By analogy, large random changes in a motor car engine would be more likely to reduce than to increase its efficiency. It is possible that a single mutation which lowered the metabolic rate,

the lif·

cally

present special difficulties for genetical analysis for two reasons. First, the continuous distribution suggests that they are influenced by genes at many different loci, and second, they may be influenced by the environment as well as by genetic make-up. For example, the flies whose survival curve is shown in Figure 1 were kept as larvae and pupae at 25°C. Flies which were kept during pre-adult life at 15°C. survived for about 20 per cent longer as adults at 25°C.

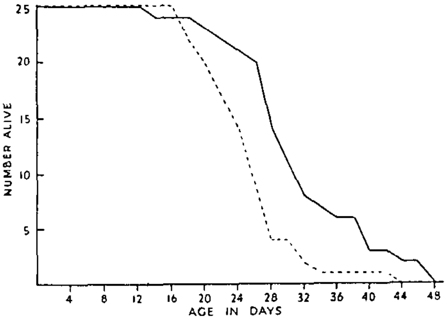


FIG. 1.—Adult survival curves at 25°C. for the F_1 hybrids between two inbred lines, B and K, of *Drosophila subobscura*. Full line, females, broken line, males

The techniques available to a geneticist in the study of continuously varying characters include in wild populations measurements of the correlation between sibs or between parents and offspring, and, in laboratory animals, investigation of the effects of changes in the breeding system, for example by inbreeding or distant hybridization, and of selection. Adult life span is in many ways an inconvenient character for such studies, since it is not known until the individual is dead. Thus selection for a shorter adult life span could be carried out only by breeding from a large number of pairs set up at random, keeping the parents until they died of old age, and [illegible]

the survivors used as parents of the next generation. There is how-

ever the danger in this procedure that maternal age itself may influence the longevity of the offspring. In parthenogenetically reproducing rotifers, Lansing (1948) showed that lines maintained from the eggs laid by young mothers could be kept indefinitely, whereas if the later eggs laid by a female were used, there was a progressive decline in mean life span in successive generations, and ... It is not known how general such an effect will ... organisms, but some special ... old idiots have a low expecta- ... the children of old mothers

For these reasons, there is less information on the genetics of ... of many other quantitative characters. However, what

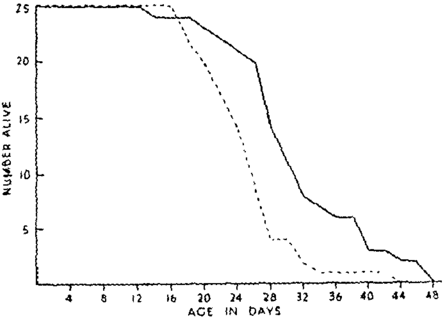
... were ... or the ... If that ... hybrids, ... d-type ... ly give

that there also exist recessive mutants for which homozygotes live

of genes at a large number of loci.

An investigation of the effects ...

present speci... First, the continu... ...influenced by genes at ma... ...ond, they may be influenced by the environm... as well as by genetic make-up. For example, the flies whose survival curve is shown in Figure 1 were kept as larvae and pupae at 25°C. Flies which were kept during pre-adult life at 15°C. survived for about 20 per cent longer as adults at 25°C.



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single locus, such that individuals with the genotype *Aa* lived ... for a short time. First, selection would ... g-lived heterozygotes, *Aa* × ... uch were short-lived homo- ... together two short-lived flies ... might give nothing but short-lived offspring (if the mating were ...

homozygous for different alleles at many of these loci, so that hybridization restores both genetic heterozygosity and long life. The ... that selection would be ineffective and that inbreeding ... pairs ... ion of ... hetero-sis", in contrast to genes with "additive" effects, in which the ...

closely associated with fitness, should show heterosis, whereas bristle number should show in the main additive inheritance. Haldane (1949) showed that in a random mating population in equilibrium under the influence of natural selection, no correlation would be expected between the fitness of parents and offspring, ...

selection, being maintained at a low frequency only by mutation. Therefore most of the genetic variance of fitness will be heterotic. It has already been pointed out that in this case there will be no ...

effects found by Lansing in rotifers operate also in *Drosophila*. The absence of any response to selection might suggest that the differences in longevity were environmental and not genetic in origin. This however is not the case. *Figure 2 shows survival curves for*

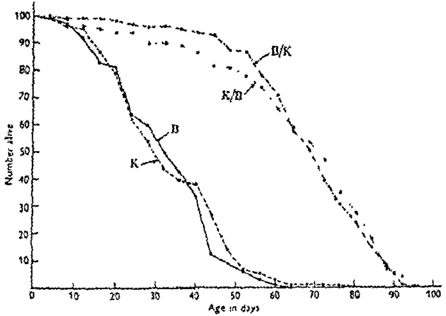

FIG. 2.—Adult survival curves (sexes combined) at 19° C for two inbred lines, B and K, of *Drosophila subobscura*, and of the F_1 hybrids between them (Clarke & Maynard Smith, 1955).

two inbred lines of *D. subobscura*, and for the reciprocal hybrids between them, kept as far as possible in identical conditions The mean expectation of life of the hybrids is approximately twice that of the inbred flies, and the difference is largely or wholly genetic. It will be recalled that Pearl also found that F_1 hybrids lived longer than their parents, but the difference in the present case was far greater, probably because the parental flies were highly inbred It should not be thought that these results demonstrate that hybridization increases the life span above that normal for the species. The offspring of fertilized females caught in the wild lived in laboratory conditions for as long as did these hybrids, although there was a small proportion of very short-lived flies among the offspring of wild females. Thus the explanation of these results is that inbreeding greatly reduced the normal life span, which was restored by crossing the inbred lines.

The simplest explanation of these facts is that genetic heterozygotes live for longer than do homozygotes. Consider what would happen if differences in longevity were due to a pair of alleles, A and a, at a

single locus, such that individuals with the genotype Aa lived

uld

×

no-

zygotes, AA or aa, whereas mating together two short-lived flies might give nothing but short-lived offspring (if the mating were $AA \times AA$ or $aa \times aa$)

mating

between

inbred lines tend to become

many of these loci, so that

hybridization restores both

heterozygote is intermediate

The

genes w

riance of the number

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main to genes with additive effects, or showing simple

fitness, *should* show heterosis, whereas bristle number should *show in the* main additive inheritance. Haldane (1949) showed that in a random mating population in equilibrium under the influence of natural selection, no correlation would be expected between the fitness of parents and offspring, although there will be a substantial

and no response to selection. To put the matter in another way, if natural selection has already

mized fitness, it is

selection. The same will be true of characters such as longevity which are closely associated with fitness, although it might be possible to increase the mean life span by selection at the expense of reduced fitness in other ways, for example reduced fertility.

There is some evidence that the genetic variance of longevity in man is in the main due to genes with heterotic effects. Beeton and Pearson (1901) measured parent-offspring and sib-sib correlations for [illegible] nsure that the [illegible] the same ecor [illegible] obtained were caused by genetic rather than environmental factors. They considered only those children who died at 21 or later, on the grounds that the causes of death in infancy and in later life are different. The mean value of the four parent-offspring correlations was 0.1365, or only about one-quarter of that for human stature, and of the three sib-sib correlations 0.2611. The higher value of the latter correlation is what would be expected from Haldane's argu- [illegible]

[illegible] of ageing is most easily studied in mammals, since too little is known of the pathology of most other groups to determine the cause of death. There is little doubt that animals of similar genotypes, kept in conditions in which there are few accidental deaths, tend to die of similar causes. For example, inbred lines of mice differ not only in the age of onset of cancers, but also in the particular kinds of cancer which develop. Similarly, different breeds of domestic dogs [illegible]

[illegible] *et al* (1954) measured the arterial pressure in the relatives of patients with "normal" blood pressures, and of patients with "essential hypertension", i.e. in patients with blood pressures higher than an arbitrarily selected value, and having no disease to which these pressures could be attributed. When allowance was made for differences due to age and sex, the blood pressures of the former group of relatives did not differ from the general population, whereas the pressures of relatives of patients with essential hypertension were higher, the excess for the relatives over the normal for their age and sex being about 20 per cent of that for the affected patients. [illegible] ination of the blood [illegible] obably in- fluenced also by environmental factors.

These results have been quoted for two reasons. First, they confirm that genetic factors influence a particular process which may

to death in old age. Second, it was found that the

may exist between expectation of life and total

the ability to withstand one particular group of

perhaps earlier in life, natural selection

the population at an optimal value If so, we

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There … longevity in man is ir… Beeton and Pearson … correlations for hum… ensure that the measured individuals were as far as possible living in the same economic conditions, and therefore that any correlations obtained were caused by genetic rather than environmental factors. They considered only those children who died at 21 or later, on the grounds that the causes of death in infancy and in later life are different. The mean value of the four parent-offspring correlations was 0.1365, or only about one-quarter of that for human stature, and of the three sib-sib correlations 0.2611. The higher value of the latter correlation is what would be expected from Haldane's argu- … ne you must

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mr…

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First, they con- … ocess which may

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DISCUSSION

N. W Pirie Was the [illegible] ... of in some other way abnormal? ... due to the community"

J Maynard Smith. The group chosen was not a random sample: it was drawn from Quaker families. The community was unlikely to have been abnormal since in the same population quite high correlation was found for other characters such as statute.

AUTHOR INDEX

The following index refers to the pages on which contributions by persons named are to be found It does not include the names of persons whose papers have been cited as references

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